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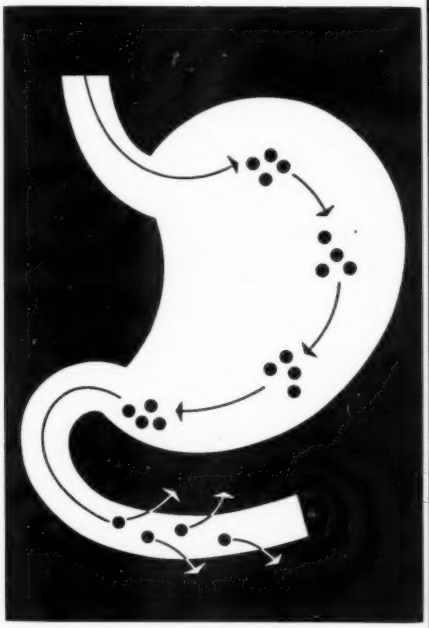

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1. Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:320, 1960.

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Information for AUTHORS

The Editors of POSTGRADUATE MEDICINE will be pleased to consider original papers in the fields of general medicine, as well as all the specialties, so presented as to be of value and interest to practicing physicians.

Papers should be typewritten, double spaced, and the original, not a carbon copy, should be submitted. Tissue weight paper should not be used. It is suggested that manuscripts comprise a maximum of approximately 3000 words. Authors' full names, academic or professional titles, and complete addresses should be given.

Bibliographies should be kept to a minimum and typed on separate sheets. References should include the author's full name, complete title of article, abbreviated name of journal, volume number, first page and year. References to books, monographs and pamphlets should include the author, title, name and city of the publisher, year of publication, edition and page number of the reference. References should be numbered consecutively throughout the paper and listed in order by number from the text.

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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants. Replies are forwarded by mail immediately and selected questions and answers are published each month in this section.

• RECURRENT CANKER SORES

Q. A 40 year old patient who wears a denture has had frequent recurrences of multiple canker sores of the gums and tongue. Treatment with a solution of 10 per cent silver nitrate, antibiotics, and weekly administration of 0.3 polyvalent influenza injection has not been effective. Could these canker sores be an allergic reaction to the denture? What treatment would you suggest?

M.D.—North Dakota

A. Contrary to general opinion, sensitivity to dentures is quite rare. Some individuals are sensitive to the monomer (liquid) used in making plastic dentures, but residual monomer is seldom present after the acrylic material has been cured.

It is highly probable that the lesions described are due to the herpes simplex virus. The weight of evidence favors the theory that most canker sores or aphthae are caused by a virus. The herpetiform lesion usually results from increased activity of the virus or reduced resistance of the cells, the herpes simplex virus being resident in the tissues without symptoms at other times. A number of factors such as infections, fevers, allergic reactions, trauma or menstruation may trigger the reaction.

Silver nitrate is contraindicated in this condition because it may force the virus deeper into the tissues and because cellular destruction results from its use.

I would suggest (1) one to two times the minimal daily dose of vitamin B complex three times a day after meals for two to four weeks (when the lesions are related to the menstrual cycle, this dosage is especially effective if the vitamins are taken for two or three days before the onset of menstruation); (2) 250 mg. of a tetracycline administered every hour hours for a period of 48 hours; (3) intradermal doses of smallpox vaccine, increasing from one during the first week to six during the sixth week; (4) withdrawal of nuts, chocolate and citrus fruits from the diet; and (5) gamma-globulin.

These measures are not to be employed simultaneously; however, if they are used in the order suggested, one of the first three will be effective in an appreciable percentage of patients. I have not had personal experience with gamma-globulin, but recent reports indicate that it has proved quite effective in a limited number of patients.

Second consultant: It is most important to determine the cause of this patient's allergic reaction to the denture, as no treatment will be effective unless the cause is removed.

The powder or paste which is sometimes used to hold the denture in place is the most common cause of allergic reaction. Some persons also are sensitive to the material from which the denture is made. These materials should be used in a patch test to determine the patient's sensitivity to them. Certain foods and the peppermint used in most dentifrices often produce reactions. A diet diary or a food-elimination regimen may reveal whether or not food is the causative factor.

(Continued on page A-20)

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References: 1. David, N. A.; Porter, G. A., and Gray, R. H.: Monographs on Therapy 5:60 (Feb.) 1960. 2. Ford, R. V.: Current Therap. Res. 2:92 (Mar.) 1960.

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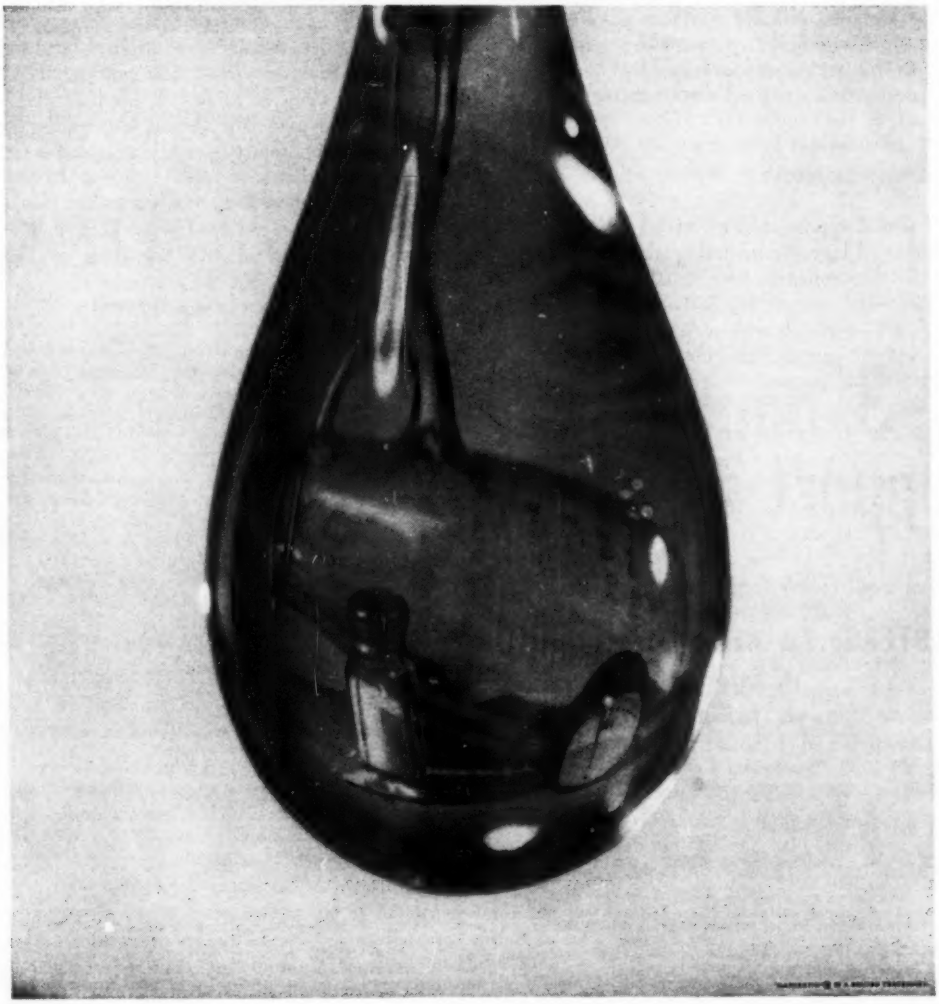

• SLEEP-INDUCING DRUGS

Q. What is an effective, safe parenterally administered preparation to induce sleep in a sick or tense postoperative patient?

M.D.—Texas

A. I most commonly use one of the barbiturates (pentobarbital sodium, secobarbital sodium or phenobarbital) to obtain rest for postoperative patients. These drugs are used to supplement rather than to replace the commonly used analgesic agents. As necessity demands, the administration of barbiturates is repeated during the night. Under certain circumstances, such as with elderly patients, chloral hydrate may be prescribed. The tranquilizing drugs are rarely used as sleep inducers and are prescribed only after barbiturates have proved unsatisfactory.

• TREATMENT OF LEPROSY

Q. I would appreciate a review of the up-to-date treatment of leprosy, including an evaluation of DDS, of thiosemicarbazone, CIBA® 1906, and of streptomycin.

What is the prophylactic value of weekly doses of DDS for people who have been exposed to the disease?

M.D.—South Thailand

A. The sulfones, particularly DDS, are considered the treatment of choice for leprosy. The life expectancy of patients with this disease has been increased, and complications have been reduced. However, since the sulfones do not always prevent ocular or bone lesions, the need for better medication is apparent. Thiosemicarbazone is of minimal value and is used only when resistance to the sulfones is evident. Streptomycin may be used in some cases of septicemia or lepra reaction, but it is of no value in routine treatment of the disease. Because Ciba 1906 has been employed for only two years, it is not possible to evaluate this drug at present. Although it does not seem to have specific therapeutic advantages over DDS, it apparently is as effective and is well tolerated by patients.

If persons exposed to contact with leprous patients cannot be removed from such contact, the oral or parenteral administration of DDS may be considered.

(Continued on page A-23)

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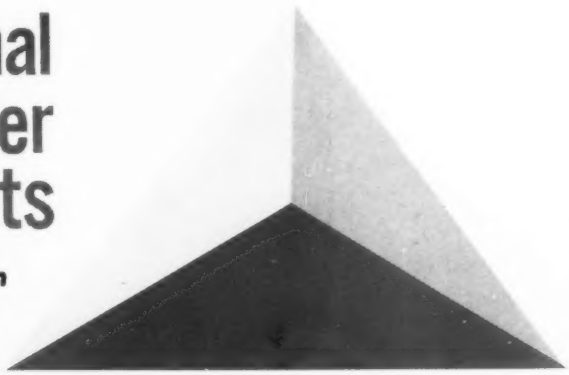

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MORE DETAILED PROFESSIONAL INFORMATION AVAILABLE ON REQUEST

• PULSE TEST FOR ALLERGIES

Q. What is the pulse test for detecting allergies? How is the test performed? Is it an acceptable method of detecting allergies?

M.D.—Pennsylvania

A. The pulse test was originated by Dr. Arthur Coca. A food to be tested is ingested, and pulse rates are recorded just before and 10 minutes after ingestion. An increase in the pulse rate ranging from more than 10 up to 30 one hour after ingestion of the food is considered to indicate an allergic reaction.

Dr. and Mrs. Coca both had allergies, and most of the research on this test was done on themselves. Their work was reported in a book entitled "Familial, Non-reaginic Allergy." For a while quite a number of allergists attempted to duplicate Dr. Coca's method, but at present I know of no one using it. In my opinion, it is not an acceptable method of detecting food allergies.

• VITILIGO

Q. A four year old girl has vitiligo on the left cheek, neck, shoulder and forearm. Her general appearance is normal and she has no other symptoms. Results of laboratory tests on blood, urine and feces are normal. Her parents and two brothers, five and six years old, are in good health.

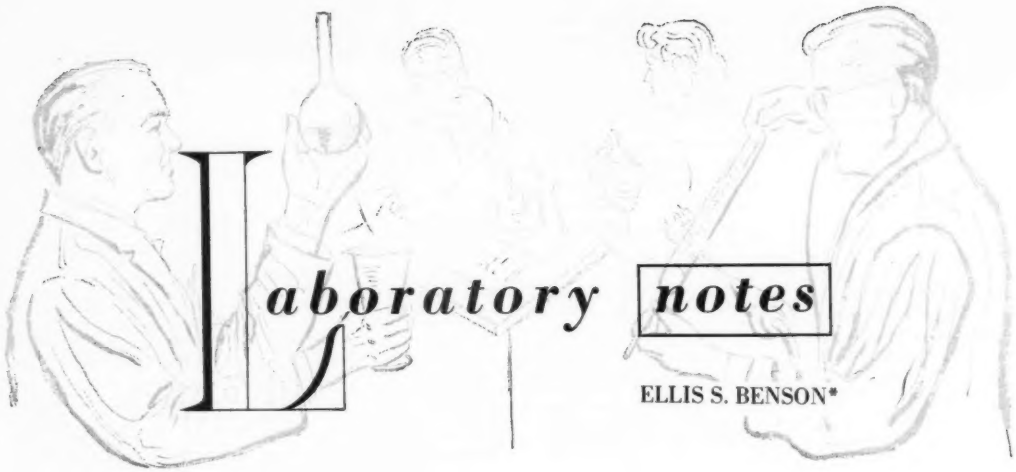
What is the cause of vitiligo and how is it treated?

M.D.—Colombia

A. Because it is rather unusual for a four year old child to have vitiligo, other diagnoses must be considered, namely, (1) tinea versicolor, caused by the fungus *Malassezia furfur*, which often produces marked depigmentation during the summer; (2) the early stage of morphea or white-spot disease; and (3) scleroderma.

True vitiligo is a lack of pigmentation; there are various theories as to its cause. It is thought that the nerve endings in the skin have a great deal to do with this condition. It is also known that some drugs, particularly those of the DIODOQUIN® group, produce depigmentation.

There is no known specific treatment for vitiligo at present. In my experience, treatment with the OXSORALEN® drugs has proved completely ineffective.



Laboratory notes

ELLIS S. BENSON*

Clinical Measurement of Erythropoiesis

R. EDWARD BELL†

University of Alberta Hospital, Edmonton

R. EDWARD BELL

In health, the body maintains a remarkably constant level of circulating red cells. Erythrocytes are continuously produced in the bone marrow; they circulate in the blood stream for a period of 110 to 120 days, and, as they reach senescence, they are selectively destroyed in the reticuloendothelial system. By regulating the cell production to a rate which is equal to that of cell destruction, the peripheral population of cells is maintained within a very narrow range. The rate of production is increased in response to increased demands for oxygen transport, such as occur at high altitude, and to compensate for loss of red cells through bleeding or hemolysis. While production of cells under these conditions may exceed for a time the rate of cell destruction, a steady state is soon reached, although this may be at a different level of hemoglobin concentration. The hormone or hormones "erythropoietin" play an important role in this homeostatic mechanism.

It is quite apparent that the level of hemoglobin or erythrocytes in health and disease is directly related to the rate of production of these cells, and quantitative estimations of the rate of erythropoiesis (and of cell destruction) in the study of patients with anemia are useful.

Methods

The methods of measuring erythropoiesis which can be applied clinically are determinations of the following.

(Continued on page A-26)

*Director of Hospital Laboratories and Associate Professor of Clinical Laboratory Medicine and of Pathology, University of Minnesota Medical School, Minneapolis, Minnesota.

†Director, Department of Clinical Laboratory Services, University of Alberta Hospital, Edmonton, Alberta.

clinical endorsement grows as proof accumulates

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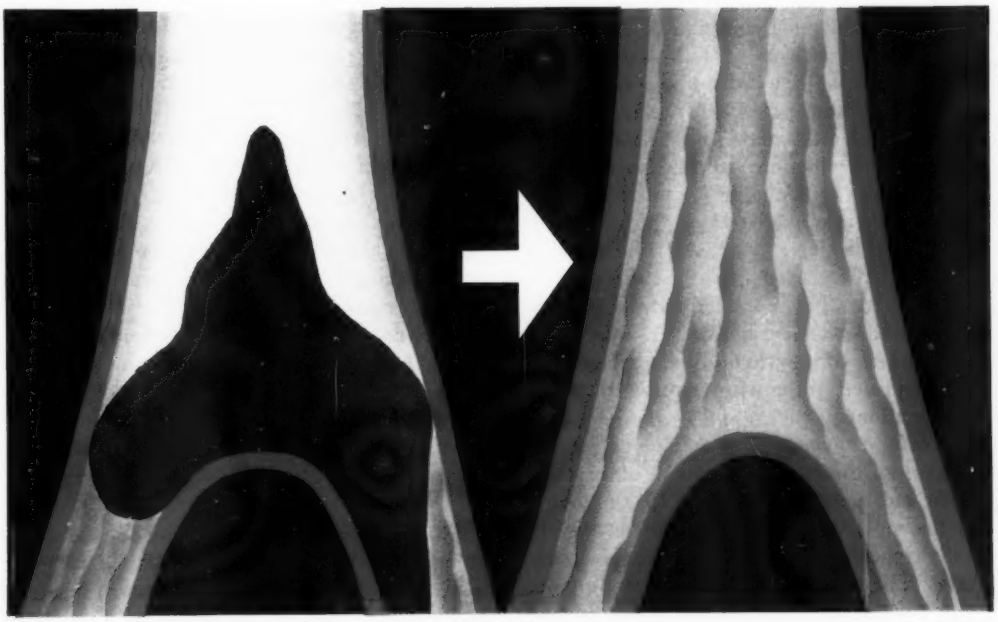

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2. Reticulocyte count.
3. Myeloid-erythroid ratio of bone marrow.
4. Iron 59 turnover in plasma.
5. Iron 59 utilization.
6. Chromium 51 erythrocyte survival.
7. Urobilinogen excretion.

Hemoglobin and hematocrit—In the assessment of erythropoiesis, the first requirement is a knowledge of the level of erythrocytes in the blood stream. The conventional methods for determining hemoglobin, hematocrit and (less reliably) the erythrocyte count provide this information. Leaving aside for the moment any consideration of the influence of fluid shifts in and out of the circulation, we may say that if the hemoglobin or hematocrit is constant, erythrocyte production is proceeding at a rate equal to the rate of erythrocyte destruction.

Since the erythrocytes live for approximately 110 days, about 0.9 per cent of them must be destroyed each day and replaced by new cells. The hemoglobin concentration and the hematocrit reflect the total mass of red blood cells; thus, they indicate a certain minimal rate of erythropoiesis that is required to maintain this total mass. For example, the erythrocyte production required to maintain a hemoglobin of 15.0 gm. is twice that required to maintain a level of 7.5 gm., provided the cells have a normal life span. If they have a decreased life span, the production rate must be proportionately greater. These measurements are, however, only useful as an index of erythropoiesis when they are interpreted in conjunction with other determinations.

Reticulocyte count—The reticulocyte count is the most direct measurement of erythropoiesis and, partly because of its simplicity, it is the most widely used. Reticulocytes are usually reported as a percentage of erythrocytes. The measurement can be made more useful by calculating the total number of reticulocytes, using reticulocyte percentage and the erythrocyte count. Reticulocytes normally constitute about 1 to 2 per cent of the erythrocytes, or approximately 40,000 to 70,000 reticulocytes per cubic millimeter.* In the vast majority of circumstances, the reticulocyte count rises in fairly direct relation to the increase in erythropoiesis. Reticulocytes are reduced in number in hypoplastic anemia and aplastic anemia. As reticulocytes are tangible evidence of new erythrocytes in the circulation, they represent effective production.

One reservation must be made regarding the interpretation of reticulocyte counts. There is a pool of reticulocytes in the bone marrow about equal to the number in the peripheral blood. Under certain conditions some of these may shift into the blood stream, and their appearance in this way does not indicate any increase in cell production. This effect is partially responsible for the very high reticulocyte counts that occur early in the treatment of pernicious anemia with vitamin B_{12}. Nevertheless, properly interpreted, the reticulocyte count is the best single available measurement of erythropoiesis; it is simply performed, reasonably accurate, and gives information not obtained by any other method.

Myeloid-erythroid ratio of bone marrow—Since the erythrocytes are produced in the bone marrow, an examination of the bone marrow might be expected to give some information regarding erythropoiesis. The erythroid precursors in the marrow are easily identified in normal health and comprise about 15 to 25 per cent of the nucleated cells in the marrow. Because of the variability of marrow aspirates, their numbers are frequently expressed as a ratio of myeloid precursors to erythroid precursors in the marrow, i.e., a myeloid-erythroid ratio. This ratio is normally in the range of from 3:1 to 4:1. Any estimate of the number or proportion of cells is only reliable if the marrow sample obtained is representative of the patient's marrow. The ratio may be great-

*Assuming a red cell count of 5 million and a life span of 120 days, the number of new cells produced each day would be $\frac{100}{120} \times \frac{5{,}000{,}000}{100} = 41{,}700$, or approximately 40,000. If they are identifiable as reticulocytes for one and one-half days, the number of reticulocytes in the blood at any time would be $40{,}000 \times \frac{3}{2} = 60{,}000$ per cubic millimeter.

(Continued on page A-28)

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ly altered by a marked change in the number of myeloid cells without a concomitant change in erythroid cells. In addition, the number of erythroid cells may be greatly increased when there is a disturbance in cell maturation, such as in pernicious anemia, without a corresponding increased delivery of erythrocytes into the circulation. The myeloid-erythroid ratio or number of erythroid precursors in the bone marrow thus reflects the total erythroid activity in the bone marrow rather than the effective production of erythrocytes.

Iron 59 turnover—In recent years there has been considerable interest in the use of radioiron (Fe^{59}) in the study of red blood cell production. One of the parameters of iron metabolism used for this purpose is the rate of disappearance of an intravenously administered dose of iron 59 from the plasma over a period of the first few hours after the injection. The iron disappears from the plasma in an exponential fashion, and the rate of disappearance appears to be related to the total mass of red cell production. The more rapid the rate of erythropoiesis, the greater the rate of loss of iron 59 from the plasma. Various indexes have been derived in an endeavor to relate these measurements more quantitatively to actual cell production. The most common of these is the plasma iron turnover, which is based on the rate of disappearance of plasma iron 59 and the total serum iron content. This is best expressed in terms of milligrams of iron turned over per hundred milliliters of whole blood per day. The normal average plasma iron turnover is 0.61 mg. per hundred milliliters whole blood per day. It reflects primarily total erythroid activity in the bone marrow.

The serum iron level and the amount of iron stores have some effect on the plasma iron turnover; an increased turnover occurs in hemochromatosis and a decreased turnover in iron deficiency. If iron deficiency can be excluded, a slow plasma iron turnover is indicative of bone-marrow hypofunction. An increased turnover occurs with increased marrow erythropoiesis, as is found in hemolytic anemia, pernicious anemia or regeneration after hemorrhage.

Iron 59 utilization—In the normal subject, 75 to 90 per cent of a dose of intravenously administered radioiron will be found in the erythrocytes within seven days after the injection. This represents iron that has left the plasma and entered the labile iron pool and the developing erythrocytes. The utilization of iron 59 so measured is low in states in which there is decreased erythropoiesis, such as in aplastic anemia and hypoplastic anemia. It is also decreased in pernicious anemia, refractory normoblastic anemia and other conditions in which there is ineffectual production of cells in spite of a marked erythroid activity in the bone marrow. The amount of iron which appears in the erythrocytes may approach 100 per cent in polycythemia and anemia due to chronic blood loss. Utilization of iron 59 is an excellent measure of the effective production of erythrocytes.

Urobilinogen excretion—Thus far, we have dealt with measurements more or less directly related to the erythrocyte production. We may obtain information on cell production indirectly by measuring the rate of cell destruction, equating the number of cells produced with the number of cells destroyed. One of the most common ways of estimating cell loss is to measure the total excretion of the end products of breakdown of the heme portion of the hemoglobin molecule, namely, urobilinogen. The total urobilinogen excretion in the stool over a suitable period of four days or more is estimated. The excretion of urobilinogen is related to the total red cell mass, and the expression of the excretion as a hemolytic index

$$\frac{\text{avg. (four days) daily output of fecal urobilinogen (mg.)} \times 100}{\text{Hb (gm./100 ml.)} \times \text{total blood volume}/100}$$

enhances the usefulness of this method. Difficulties are often encountered in getting complete stool collections, and this reduces the value of the method to some degree. In addition, a fraction variously estimated at between 10 and 20 per cent of the pigment is not related to red cell breakdown but arises through some other pathway in bile pigment metabo-

(Continued on page A-30)

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lism. Nevertheless, when rapid erythropoiesis is compensating for rapid cell destruction, such as in hemolytic anemia, the amount of urobilinogen in the stool is increased above normal, roughly in proportion to the increased rate of destruction and of production of erythrocytes.

Erythrocyte survival (chromium 51)—This is another method which indirectly gives information on the rate of erythropoiesis through the measurement of erythrocyte destruction. The life span of the erythrocytes can now be determined quite conveniently by using radiochromium (Cr^{51}) as an erythrocyte label. Destruction rates of 1.5 to 2 times normal or more can be quite reliably estimated; from this the corresponding rate of erythropoiesis is inferred. Although the information obtained is only indirect, it is an exceedingly useful measurement of the effective rate of erythrocyte production, particularly in hemolytic anemia.

Effectual Vs. Ineffectual Erythropoiesis

The methods discussed measure different parameters of erythropoiesis. They can be divided into two groups, depending on whether they measure effectual or ineffectual erythropoiesis. In some circumstances, erythropoiesis, although very active (as shown by increased numbers of developing red cells in the marrow, increased total urobilinogen excretion, and rapid plasma iron turnover), does not appear to influence the level of hemoglobin, reticulocytosis or iron utilization. Perhaps the best illustration of this state occurs in untreated pernicious anemia, in which an extremely active erythropoietic marrow, rapid plasma iron turnover, and increased urobilinogen in the stool (all indicating increased erythropoiesis) are associated with a deficiency of erythrocytes reaching maturity. The term "ineffectual erythropoiesis" has been applied to this observation. This is in contrast to the situation in hemolytic anemia, in which, in addition to increased erythropoiesis (as indicated by erythroid hyperplasia in the bone marrow, rapid plasma turnover, and increased urobilinogen excretion), there is also a reticulocytosis, high iron utilization, and rapid turnover of erythrocytes (as estimated from their abbreviated life span). This concept helps to explain some of the apparent inconsistencies found in applying these methods to clinical medicine.

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- A suction catheter of inert and hydrophobic SILICONE® rubber has been used in an attempt to provide better drainage of wounds involving medullary bone where complete hemostasia cannot be achieved by ordinary technics. The volume of drainage was 405 ml. in 26 hours, the catheters being withdrawn when no significant amount of fluid was obtained. A follow-up of 100 such cases showed a more benign afebrile postoperative course and a lowered incidence of wound complications.—Dr. Theodore R. Waugh, New York.
- Arthrodesis of the hip is the procedure of choice for most active young and middle-aged persons who require extensive surgical reconstruction of the hip, provided the opposite hip, the lumbar part of the spinal column, and both knees are normal.—Dr. Paul R. Lipscomb, Mayo Clinic, Rochester, Minn.
- An analysis of 82 cases of fractures of the os calcis and a follow-up evaluation of 44 fractures for an average of five years showed that the maximal improvement may not be reached for two or three years. Late functional results were usually much better than early results.—Dr. Louis J. Levy, Fort Worth.

CERULOPLASMIN IN DISEASE

Conference on Plasma Proteins:

- The total concentration of plasma ceruloplasmin, and thus plasma copper, rises as the result of many diseases, including infection, myocardial infarction, lymphoma and hyperthyroidism; following the administration of estrogens or androgens; and in late pregnancy. It decreases in patients who lose the protein in urine or stools, in some patients who have intestinal malabsorption, and in patients who have inherited an inability to synthesize normal amounts of this protein and in whom Wilson's disease eventually develops.—Dr. I. Sternlieb, Albert Einstein College of Medicine of Yeshiva University, New York.

TEST FOR ABO RISK

American Society for Hematology:

- Preliminary observations suggest that ABO erythroblastosis is dependent on 7S antibodies that are resistant to neutralization by specific soluble blood group substances, and that a satisfactory prenatal test for detecting the possibility of ABO disease may be available.—Dr. R. E. Rosenfield, Mount Sinai Hospital, New York.

Thyroid surgery urged

Western Surgical Association:

• Early prophylactic subtotal thyroidectomy in all patients with nontoxic nodular goiters or adenomas is the most effective treatment of carcinoma of the thyroid. In a 17 year period, 57 malignancies were found in 728 patients undergoing surgery for nontoxic nodular goiter.—Dr. Robert C. Surridge, Los Angeles.

ICF substance in arthritics

American Rheumatism Association:

• An inhibitor of complement fixation, apparently specific for rheumatoid arthritis but different from the rheumatoid factor, has been found in the blood of 50 patients with rheumatoid arthritis and in some patients with systemic lupus erythematosus and scleroderma. The ICF substance interferes with the normally prompt interaction of the complement system and the antigen-antibody reaction. Substances similar to ICF occur in healthy individuals, but are less potent than in persons with rheumatoid arthritis.—Dr. Ralph Heimer, Hospital for Special Surgery, New York Hospital-Cornell Medical Center, New York.

• No cases of polyneuropathy were found in 5,188 patients with rheumatoid arthritis examined during the presteroid era of 1945 to 1949. Sixty-one cases were seen from 1950 to 1960. The majority of these patients had received heavy doses of corticosteroids. Relative adrenal insufficiency resulting from stress or reduction of dosage may set the stage for the appearance of polyneuropathy.—Dr. Richard H. Ferguson, Mayo Clinic, Rochester, Minn.

• A study of 91 blood relatives of 24 patients with scleroderma gave additional support to the belief that scleroderma occurs in families which have a genetic predisposition to abnormalities of immune systems.—Dr. J. M. Corcos, New York.

Antibodies to enzymes

Conference on Multiple Molecular Forms of Enzymes:

• The tissue source of enzymes in blood may be determined, and such information may be of diagnostic value. Patients with skeletal metastases have an increased proportion of serum alkaline phosphatase precipitable by an antibody to bone phosphatase and a decreased proportion precipitable by an antibody to intestinal phosphatase. On the average, about 26 per cent of serum lactic dehydrogenase in normal persons is found to be inhibited by an antibody to liver enzyme. In patients with infectious hepatitis or homologous serum hepatitis, the fraction inhibited rises above 60 per cent and recedes to normal levels when the disease abates.—Dr. J. S. Nisselbaum, Sloan-Kettering Institute for Cancer Research, New York.

"Interpretive cortex" details the past

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• A large part of the covering of the temporal lobe may be called the "interpretive cortex." Functionally, it may be considered to belong to a different integrative level than the so-called sensory cortex and motor cortex, because it deals with records of experience which have already passed through the mind. Gentle electric current applied to the area of the cortex permits recall in far more detail than any person could summon voluntarily. It is apparent that when a present experience resembles an experience from the past, that past is summoned automatically as a reflex. An individual is not aware of the summoning until the realization that the situation is familiar or dangerous flashes up in his consciousness.—Dr. Wilder Penfield, Montreal Neurological Institute, Montreal.

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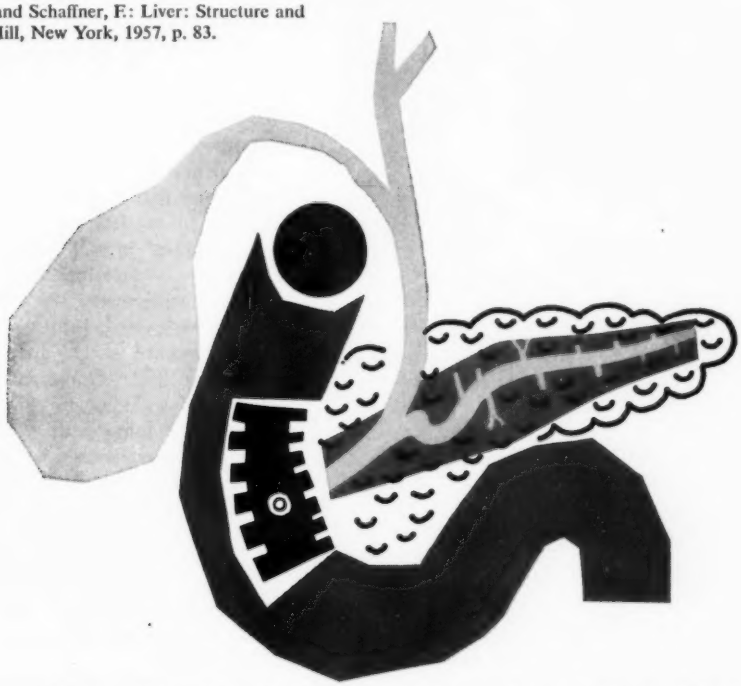

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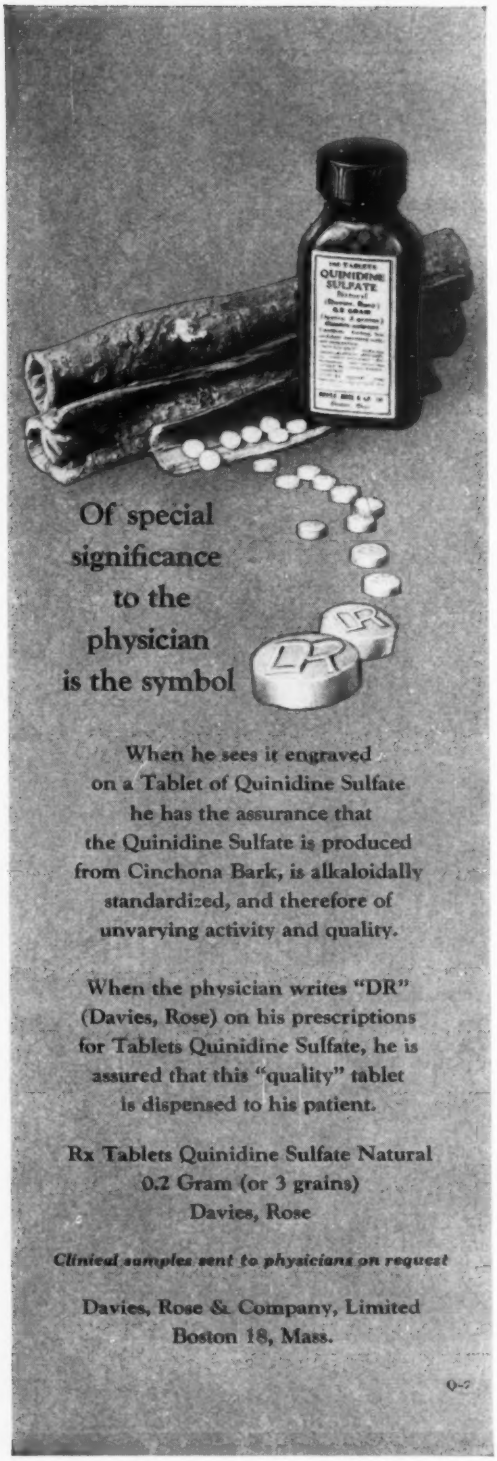
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The Editor's Mail

FLUORESCENCE EQUIPMENT

To the Editor:

In response to my article "Fluorescence microscopy for cytodiagnosis of cancer" in the December 1960 issue of Postgraduate Medicine, I have received many letters from readers inquiring about sources for fluorescence lamps. I have replied to each of these letters and have supplied additional material on the fluorescence method. Since more readers may wish to use fluorescence cytodiagnosis in their practice and may have difficulties in locating firms which supply fluorescence equipment, the following information may prove to be helpful.

Fluorescence lamps are standard equipment, being used, for example, in immunologic studies. For the cytodiagnostic fluorescence method, a fluorescence lamp with a high-pressure 200 W mercury burner is used with any standard microscope. Exciter and barrier filters are furnished with the lamps. No special microscope objectives are necessary.

In addition to supplying fluorescence equipment, the following firms also supply excellent microscopes.

American Optical Company, Buffalo 15, New York

William J. Hacker & Co., Inc. (Reichert), P.O. Box 646, West Caldwell, New York

E. Leitz, Inc., 468 Park Avenue South, New York 16

Wild Heerbrugg Instruments, Inc. (Wild), Main and Covert Streets, Port Washington, Long Island, New York

Carl Zeiss, Inc., 485 Fifth Avenue, New York 17

Excellent for use in the fluorescence method are two preparations, G. T. Gurr's and Michrome acridine orange. Both are available from ESBE Laboratory Supplies, 459 Bloor Street West, Toronto, Ontario. Michrome acridine orange is also available from K & K Laboratories, Inc., 177-10 93rd Avenue, Jamaica 33, New York.

Sincerely yours,
Felix D. Bertalanffy, Ph.D.
Winnipeg, Manitoba

Radiology FOR PRACTICING PHYSICIANS

PAUL C. HODGES*

Arteriography of the Extremities

S. I. SELDINGER

Karolinska Sjukhuset, Stockholm, Sweden

Dr. Sven Ivar Seldinger has worked for many years in the central department of diagnostic radiology, Karolinska Sjukhuset, Stockholm, Sweden. His scientific interests are primarily concerned with arteriography. He is a recognized authority in this field.—Paul C. Hodges, M.D.

THE extensiveness and site of arterial calcifications can be determined by plain roentgenography. The type of calcification occurring in the vascular wall can be determined also by this method (figure 1). Intimal and medial calcifications in the arteries have a characteristic appearance on the roentgenogram which is important; the former, but not the latter, are suggestive of stenosis. For closer study of the arteries of the extremities, however, angiographic examination is necessary.

After three decades of development, arteriography of the extremities today is a relatively simple examination. It is almost always possible to inject the contrast medium into the artery after percutaneous puncture. The best

S. I. SELDINGER

puncture site in the upper extremities is in the brachial artery at the antecubital fossa; in the lower extremities, the best site is the femoral artery close to the inguinal ligament (figure 2). With some training, the physician generally can puncture the brachial artery quite easily. The femoral artery is as easy to puncture as is a superficial vein. When these puncture sites are used, the subsequent introduction of a catheter is sometimes necessary to achieve an adequate vascular level for the injection of contrast medium, e.g., in examination of the pelvic and shoulder arteries or of obliterations situated proximal to the previously mentioned sites of puncture (figure 3). As rapid injection of the contrast medium is necessary, the catheter must have a comparatively large lumen. A catheter of maximal thickness in relation to the needle can be

*Emeritus Professor and Chairman, Department of Radiology, University of Chicago, Chicago, Illinois.

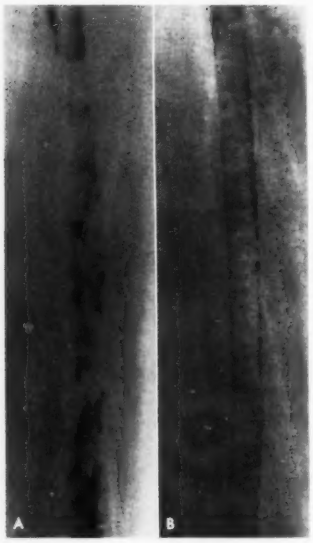

FIGURE 1. Intimal (A) and medial (B) calcifications of the femoral artery.

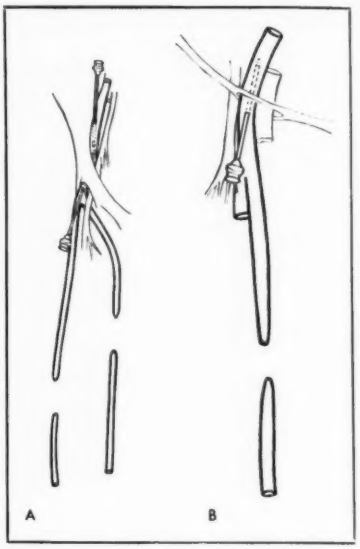

FIGURE 2. Drawings of the most suitable sites for puncture of the arteries of the extremities.

A. Brachial artery at passage beneath the bicipital aponeurosis. Surrounding structures include the concomitant veins and the median nerve.

B. Femoral artery at passage beneath the inguinal ligament. Surrounding structures include the femoral vein (medial to the artery) and the femoral nerve.

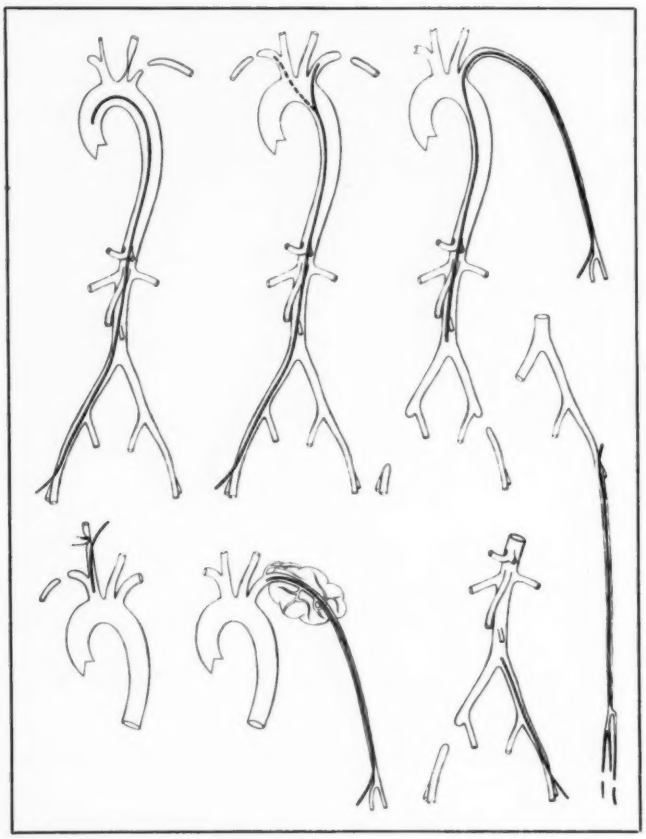

FIGURE 3. Drawings of different possible sites for percutaneous catheterization when arterial obliterations or other lesions are unfavorably situated in relation to suitable puncture sites.

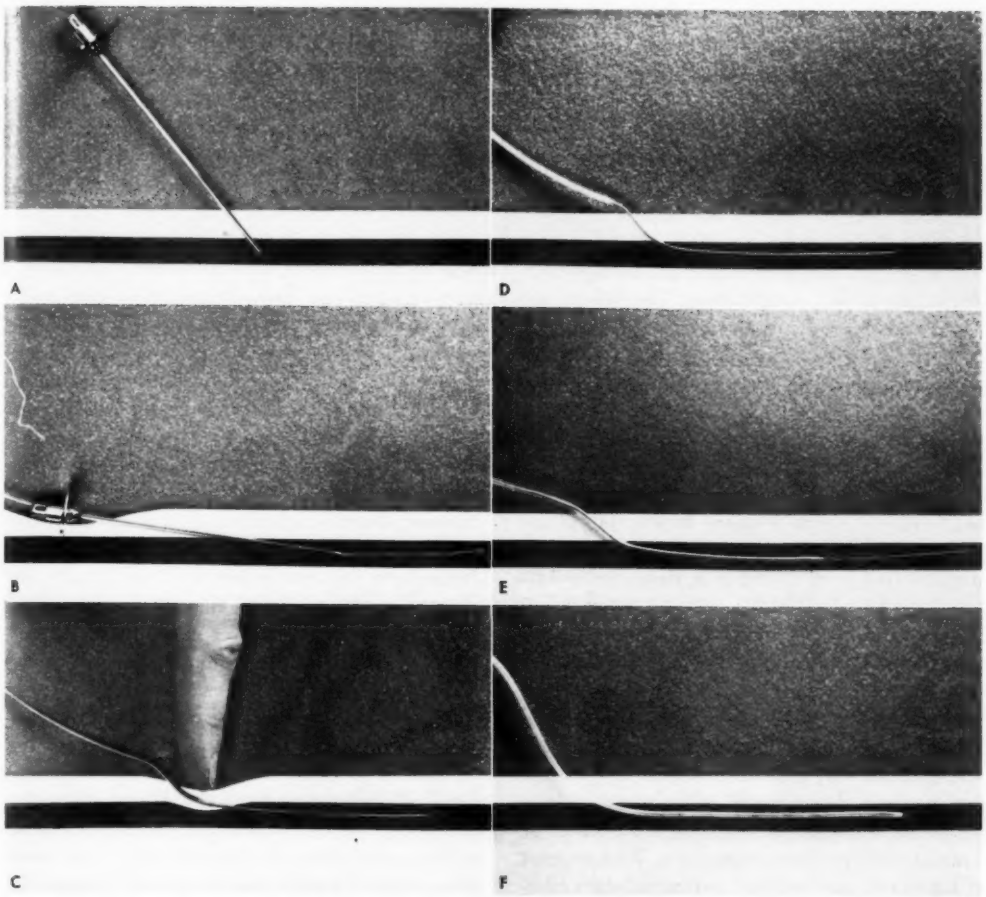

FIGURE 4. Method of introducing into an artery a catheter which is of the same size or larger than the puncture needle or cannula used.

A. The artery is punctured percutaneously and the stylet is withdrawn from the cannula.

B. The cannula is advanced into the arterial lumen, and a semiflexible metal guide is introduced through it.

C. The cannula is withdrawn from the guide; the latter is kept in place. Compression is applied over the puncture hole to prevent bleeding.

D. A polyethylene catheter is threaded onto the guide. The tip of the tubing is molded to fit exactly around the guide.

E. The catheter is introduced into the artery, advanced by the guide. The puncture hole is covered, and bleeding is prevented.

F. The guide is withdrawn.

easily inserted into the artery after removal of the needle (figure 4).

The flow in peripheral arteries is considerably less than in the large central vessels. Therefore, when contrast medium is injected into such arteries (or into the aorta close to the bifurcation), it is not necessary to use a pressure apparatus for the injection or a mechanical film changer for the exposures. Serial film exposures are necessary, but a simple,

manual cassette changer, permitting exposure of three to four films at intervals of two to three seconds, is sufficient for most purposes.

In arteriography, the puncture and injection of contrast medium should be performed by the roentgenologist, and this procedure can very well be combined with the planning of technical details such as the choice of exposure data, projection, etc. It is obvious that the person who must interpret the films should also perform the examination. The procedure of puncturing and catheterizing arteries is not so difficult that it cannot be performed by every physician of average manual ability, whatever his specialty.

If a contrast medium of the diatrizoate type is used in arteriography, the patient experiences only moderate, quite tolerable discomfort. This is because these media (UROGRAFIN®, HYPAQUE®) cause so little irritation. A suitable dosage of contrast medium for arteriography of the extremities is generally 10 to 30 ml. of 45 to 60 per cent solution in each injection, depending on the place of injection. Each injection is made so as to fill as few as possible of the arteries unimportant to the examination. Selective arteriograms obtained in this way have an incomparably better quality than those made with injection into the aorta, even when very large amounts of contrast medium have been used. With repeated injections and correct puncture and catheterization technic, large vascular areas can be examined by a series of such selective arteriograms made on one occasion.

The smallest arteries that can be distinguished in an arteriogram of a living person have an inside diameter of about 0.1 to 0.3 mm., depending on the depth of the region photographed. This fact indicates what arterial lesions may be diagnosed by this method. In the individual arteries, if they are sufficiently large, stenosis and obliteration, dilatation, dislocation or other pathologic conditions and distribution may be observed. If they are sufficient in number, vessels with smaller dimensions than those indicated may be indirectly revealed by a more rapid arteriovenous passage of contrast medium than is normal; they also may cause a visible, diffuse accumulation of contrast medium to be present in the tissue (figure 5).

By far the most important indication for arteriography of the extremities is arterial stenosis. In this condition, as in others, new therapeutic possibilities often demand better methods of examination. Thus, the rapid development of reconstructive arterial surgery has increased the indications for arteriography and thereby encouraged refinement of arteriographic technic. Emboli, thrombi and aneurysms can be removed. The arterial blood stream in an extremity with a stenosal main artery can be restored by grafts consisting of autogenous veins, homologous arteries or synthetic material.

Localization of an acute obstruction (figure 6) is therefore sometimes necessary, but chronic stenosis, which is, as a rule, combined with inveterate thrombosis, is generally the indication for arteriography. The causes of thrombosis vary, but in the great majority of cases, at least in the lower extremities, atherosclerotic changes are responsible. An extensive, high degree of atheromatosis increases the risks of postoperative recurrent thrombosis (figure 7). However, by using the bypass technic, with introduction of transplanted material at a distance from the obliteration, the blood can be led past highly changed areas; at the same time, all the collaterals that have been formed earlier can be saved (figure 8). By this method, much can be gained and little is lost.

In order to determine the most suitable site for implantation and to choose the appropriate operative technic, the entire arterial system of the extremity must be mapped out. Widespread lesions in the arteries of the pelvis and lower leg may contraindicate operation for an obliteration in the femoral artery. The capacity of the collaterals should be elucidated, and a suitable place for implantation indicated (figures 7 and 8).

Some other stenosing arterial diseases that are much less common than atherosclerosis are also of great interest to the surgeon and therefore to the roentgenologist, since they are particularly suitable for reconstructive operation. As may be expected, the best results are

FIGURE 5. A. Plain roentgenogram of a giant-cell tumor of the radius.

B. Arteriogram of the same tumor. The contrast medium is diffusely dispersed in the tumor, due to an extensive number of capillaries. There is contrast medium in efferent veins before afferent arteries are emptied, indicating rapid arteriovenous passage. (a = artery; v = vein.)

FIGURE 6. An embolus impacted at the bifurcation of the brachial artery (e). There is no contrast medium in the radial artery, while the ulnar and interosseous arteries are well filled. There is an extensive periarticular collateral network.

Rapid passage of contrast medium into a large vein (v) is due to increased peripheral arterial resistance. Part of the brachial artery is narrowed, which is caused by spasm induced by catheterization. (c = catheter.)

obtained in a short, solitary obliteration in an otherwise healthy artery. This condition may be found, for instance, in posttraumatic thromboses in young people, sometimes when a thrombus has developed in conjunction with an aneurysm (figure 9), and in so-called cystic adventitial degeneration, which hitherto has been found only in men (figure 10). Some other diseases producing stenosis in younger patients are less suitable conditions for operation because of their multiple and progressive character. Among these is the so-called branchial arteritis (brachiocephalic arteritis or Takayasu's disease), which is discovered more and more often in young and middle-aged women and is a panarteritis in the aortic arch and the proximal parts of its large branches. Another such disease is thromboangiitis obliterans, which occurs almost exclusively in young men, and is seen chiefly in the arteries of the lower leg (figure 11).

Arteriography can reveal the existence of arteriovenous shunts. The pathologic arteriovenous communication can be traumatic or congenital (figure 12). Shunts also occur in some hemangiomas (figure 13) and tumors of nonvascular origin (figure 14A). Clinically, it may be difficult to distinguish between hemangiomas and pure congenital arteriovenous fistulas. As the congenital fistulas frequently give rise to tangled masses of tortuous, widened afferent and efferent vessels, the exact arteriographic localization of the fistulas generally is impossible. The differentiation of hemangiomas also may be difficult. More significant than such differentiation, however, is generally the question of whether or not an important shunt is present. Arteriography provides better possibilities of answering that question than does any other examination, including biopsy. If considerable shunts are present, serious pathologic growth and nutritional disturbances can occur in the limb. If the operative treatment is to succeed, all the supplying arteries must be injected with contrast medium, and the whole vascular area containing

FIGURE 7. A. Extensive atherosclerosis of the femoral artery, which is most severe in the adductor channel, in which there is also a complete obliteration due to thrombosis.

B. Arteriogram after end-to-end anastomosis had been performed with an autogenous venous graft. (Graft was made between top and bottom arrows; middle arrow indicates a venous valve.) The collateral arteries filled with contrast medium decreased in number and diameter after operation. There is still severe atherosclerosis in the artery furnishing the main blood supply to the leg, and recurrent obliterating thrombosis will very likely occur.

FIGURE 8. Atherosclerotic obliteration of the femoral artery, due to thrombosis in the adductor channel. End-to-side anastomosis with an autogenous venous graft is performed. Severe atherosclerosis is present in the blind arterial sac, but not in those parts of the artery which are still the main source of blood supply to the leg.

FIGURE 9. Obliteration of the popliteal artery, due to thrombosis arising in an aneurysm. The latter is not filled with contrast medium because of the thrombosis, but it causes dislocation of the artery, the upper and lower parts of which do not form a continuous line. The artery is otherwise unchanged. The leg is supplied with blood via the sural arteries exclusively.

FIGURE 10. Cystic adventitial degeneration causing stenosis of the popliteal artery. A mucinous cyst in the adventitial layer decreases the lumen and increases the outside diameter of the artery. The artery is otherwise unchanged.

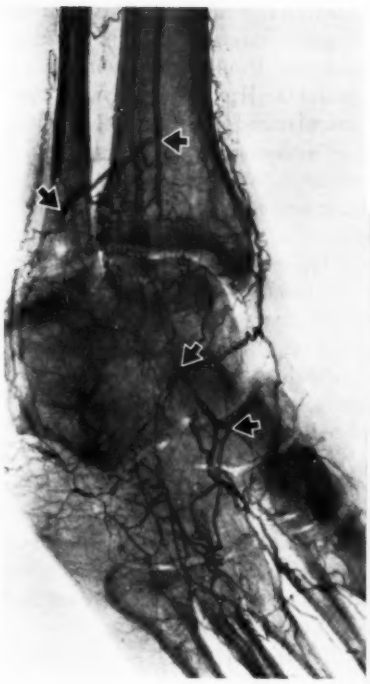

FIGURE 11 (*left*). Malleolar and tarsal arterial pattern in a case of thromboangiitis obliterans. The anterior tibial and fibular arteries are obliterated in the calf; the posterior tibial artery is obliterated above the ankle (top arrow).

The limits of some of the multiple obliterations are indicated by arrows. The open parts of the arteries have smooth, even contours. The formation of collaterals with typical tortuous appearance is extensive.

FIGURE 12 (*center*). Vascular pattern associated with congenital arteriovenous fistulas. There is increased length of bones in the fistular area, particularly of the second metacarpal. Rapid arteriovenous passage of contrast medium is indicated by its simultaneous appearance in arteries and veins.

The interosseous (ai) and the radial (ar) arteries have been ligated, but the blood has again made its way to the fistulas through collaterals between the two. Arteries and veins are difficult to differentiate. The widening of these vessels, particularly of the arteries, indicates increased flow. The separate fistulas are not to be localized.

FIGURE 13 (*right*). Cavernous hemangioma. There is rapid arteriovenous passage of contrast medium, but the normal size of the artery indicates less flow than in the case illustrated in figure 12.

The hemangioma is incompletely filled, and the phleboliths show that thrombosis is present. (a = artery; v = vein; c = irregular venous cavities; ph = phlebolith.)

FIGURE 14. A. Highly malignant fibrosarcoma with a high degree of shunting and numerous pathologic vessels. The most suitable area for biopsy (m) is the region in which the vessels are most numerous, which is probably the most malignant part of the tumor. (a = artery; v = vein.)

B. Fibrosarcoma with a low degree of malignancy (fibromatous tumor with local malignancy). The arteries are displaced, but there are no more vessels than in the surrounding structures. Spastic contractions of the artery were initiated by the puncture and catheterization.

the shunts must be arteriographically mapped out. If any shunts are left at operation, they grow quite rapidly and pathologic conditions recur (figure 12).

Arteriovenous shunting of the blood occurs also in certain malignant tumors and is caused by numerous thin-walled pathologic vessels in the tumor. Such an abundance of pathologic vessels and such a high degree of shunting in an extremity as seen in figure 14A practically prove that the tumor is malignant. These findings are observed in arteriograms of highly malignant mesenchymal tumors, such as osteogenic sarcoma and fibrosarcoma, and in metastases from hypernephroma and thyroid carcinoma. Highly malignant tumors are more vascularized than are those with a low degree of malignancy, and the most highly malignant areas in the tumor are also those with the most vessels. Thus, with the aid of arteriography, the correct location for biopsy (the site of highest vascularization) can be indicated; the treatment should be influenced by the highest degree of malignancy within the tumor region. Preferably, the degree of malignancy should not be judged in radiation-treated tumors, since the vessels are more or less normalized by the radiation.

A more moderate hypervascularity and shunting can be observed in tumors of either a low degree of or doubtful malignancy and in chronic inflammation. When the phenomenon is observed in an extremity in malignant epithelial tumors other than metastases from hypernephroma and thyroid carcinoma, it may mean that the tumor is surrounded by secondary chronic inflammation, which is not unusual. As a rule, benign tumors (apart from vascular tumors) have no more vessels than does the surrounding tissue (figure 14B).

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Numerous investigators have shown that the absorption of oral antibiotics varies not only from subject to subject, but also in the same subject at different times. To provide a high degree of therapeutic assurance, therefore, requires an antibiotic that is on the average well absorbed. High absorption, of course, implies high serum concentrations which, in turn, means an increased likelihood that tissues will be supplied with adequate antibiotic.

The absorption of phenethicillin potassium (DARCIL) has been investigated both by studies of serum concentrations and urinary excretion rates.

Maximum Absorption Indicated by Prompt, High Peak Serum Levels. Blood level studies demonstrate the reliable absorption of phenethicillin potassium. In studies employing single oral doses of 250 mg. of phenethicillin potassium, Morigi and associates[1] determined that peak serum levels of the antibiotic were attained within an hour after ingestion; assayable levels were maintained for 4 to 6 hours. Knudsen and Rolinson,[2] among others, have also demonstrated that phenethicillin potassium produces unusually high blood levels.

Serum Levels Directly Reflect Dose Levels. Cronk and associates performed an interesting experiment that emphasizes the absorption of phenethicillin potassium. Phenethicillin potassium was given to healthy adults in progressively increasing doses. *The resultant serum levels were directly proportional to the doses given.*

Average Serum Concentration ½ Hr. after Administration

Dose (Mg.)	*Mcg./Ml.*	*Units/Ml.*
134	2.72	4.35
268	4.28	6.85
536	8.15	13.0
804	12.3	19.7
1072	19.1	30.6
2144	39.6	63.4

Therefore, when treating a patient with a severe infection, the physician may, by adequately increasing the dose, produce serum concentrations that should be sufficiently great to affect less susceptible pathogens.

Excellent Absorption Indicated by Urinary Excretion Studies. Knudsen and Rolinson,[2] in a study of 9 fasting subjects, reported that a mean of 60% of the dose of phenethicillin potassium was excreted in the urine within 6 hours after ingestion of the drug. Cronk and associates found a lower, although still high, rate: 24 to 35% of a given dose of phenethicillin potassium was excreted in the first 6 hours; almost three quarters of this percentage was excreted in the first 2 hours alone. Morigi and associates[1] collected urines of 10 healthy subjects at 6-hour intervals following a dose given one hour before meals. As can be seen, the excretory rate of phenethicillin potassium reflects prompt absorption and utilization.

Average Urine Concentrations Following a Single Oral Dose of 250 mg. Phenethicillin Potassium

	0-6 Hrs.	*6-12 Hrs.*	*12-24 Hrs.*
phenethicillin potassium	30.9%	0.4%	0%

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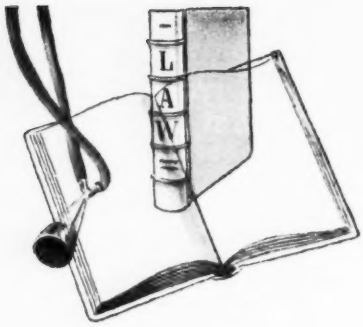
SUPPLIED: DARCIL Tablets (peach colored, scored)—250 mg. (400,000 units), 125 mg. (200,000 units) phenethicillin potassium, bottles of 36 and 100. DARCIL for Oral Solution—125 mg. (200,000 units) phenethicillin potassium per 5 cc. teaspoonful, bottle of powder to be reconstituted to 60 cc.

Although infrequent, adverse reactions to many modern drugs may occur. For further information on limitations, administration and prescribing of DARCIL, see descriptive literature or current Direction Circular.



Forensic Medicine

OLIVER C. SCHROEDER, JR.*

Estimating Time of Death

WILLIAM HOFFMAN†

Cuyahoga County Coroner's Office, Cleveland

Editorial Comment

Basically, the law is interested in events, happenings and incidents. With such human experiences, legal rights and duties are altered. Death is a very important legal event. About 20 per cent of the deaths in the United States are obscure, unexplained, unexpected or violent. The time of these deaths not only aids in determining their cause but also provides a crucial fact for solutions to legal conflicts.

When did the homicide victim die? In State v. Sheppard, 100 Ohio App. 345, 128 N.E. 2d 471 (1955), time of death became important as circumstantial evidence against the accused because he could not explain his delay of from 45 minutes to two hours in summoning police to the scene of his wife's murder. A similar use of time of death was made in State v. Petro, 148 Ohio St. 505, 76 N.E. 2d 370 (1947) and in Pruitt v. State, 270 Pac. 2d 351 (Okla. Criminal Court of Appeals, 1954).

When did the insured die? A life insurance policy was valid only when accepted by the insurer in the insured's lifetime (Metropolitan Life Ins. Co. v. James, 225 Ala. 561, 144 So. 33 [1932]).

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When did an intoxicated husband die? If he died within a few hours after being served liquor by a dramshop operator and the intoxication became the cause of death, the widow can recover damages and loss of means of support against the tavern keeper in some states (Hocker v. O'Klock, 16 Ill. App. 2d 414, 148 N.E. 2d 618 [1958] and Zahn v. Muscarello, 336 Ill. App. 188, 83 N.E. 2d 504 [1948]).

When did a joint tenant owner of real estate die? The whole title to the realty passes to the other joint tenant who survives, albeit for only a few hours (Thomas v. Anderson, 215 P. 2d 478 [4th Dist. Ct. of App., Cal. 1950]).

An interesting fact is that the law accepts the medical definition of death. In the third edition of "Black's Law Dictionary," death is defined as ". . . the cessation of life; the ceasing to exist; defined by physicians as a total stoppage of the circulation of the blood, and a cessation of the animal and vital functions consequent thereon, such as respiration, pulsation, etc.

"While it may be said that persons who are alive at the same time are living simultaneously, death occurs precisely when life ceases and does not occur until the heart stops beating and respiration ends. Death is not a continuing event and is an event that takes place at a precise time."

This harmony of law and medicine in defining the time of death is encouraging. The need of scientific evidence to determine the estimated

(Continued on page A-62)

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time of death is crucial in solving the complex legal problems of modern society. Dr. Hoffman's basic article will (1) refresh the recollection of physicians on this important subject, (2) provide a check list for scientific decision, (3) encourage local medical societies to improve the scientific methods of estimating the time of death within their communities, and (4) offer to lawyers opportunity to utilize the knowledge of medical experts in pursuit of truth—Oliver Schroeder, Jr.

WILLIAM HOFFMAN

WE can emphatically state that the sooner after death we can examine a body, the more accurately we can estimate the time of death.

We can define death as the absence of life, that is, the absence of metabolism. Death produces many signs. Early postmortem changes occur when the oxygen cycle stops. Highly specialized tissue, such as the brain and spinal cord, perish rapidly. The heartbeat and breathing cease; the blood stops flowing. Chemicals in the tissues which have been held in check by other chemicals during life now act unopposed and begin to destroy the tissues. This destruction can be noted within 24 hours after death. These tissues become discolored. Perforations of the stomach and esophagus will eventually occur. Clots will form in the heart and blood vessels, due to settling out of the elements composing the blood.

Exterior Signs of Death

The most reliable signs of death are those seen by examining the exterior of the body.

Loss of movement—Although loss of movement is the earliest sign of death, caution is required in regarding this sign as such, since corrosive and other poisons, drowning, electrocution, or comas in insane persons can cause severe shock and depress the body.

Cessation of heart action and respiration—The only reliable sign of death in the early postmortem stage is the cessation of heart action and respiration. The best examination to determine whether or not this has occurred is to listen with a stethoscope over the chest and over the larynx, where the breath sounds can best be heard. A mistake is rarely made with this method.

Loss of body heat—After death, heat production ceases in the body. The temperature is gradually lowered to that of the external environment. The rate of heat loss is not uniform and depends on many factors. The more exposed parts, such as the hands and face, lose heat more quickly, depending on the external temperature. These parts may feel cold while the internal organs are still warm. Generally speaking, a small, poorly developed body, especially if nude, will lose heat more rapidly than will a large, fat body, especially if fully clothed. A body exposed to the sun will feel hotter than normal, while one exposed to zero weather will freeze quickly, due to formation of ice in the blood vessels and the body cavities. Acute infections will produce a high temperature that may last many hours after death. Generally speaking, the body temperature drops 1° C. per hour and takes about six to eight hours to reach the temperature of the external environment.

Postmortem lividity—A purplish-red discoloration appears after death in the dependent parts of the body. It is caused by cessation of circulation, stagnation of blood, and settling of the blood by gravity. The position of the corpse determines the site of lividity. Sometimes, the pressure of gravity produces rupture of tiny blood vessels, causing pinpoint hemorrhages to appear. Livor mortis usually appears from 20 to 60 minutes after death in normal people, and about one to four hours after death in anemic people. It is usually complete in 12 hours. In deaths by asphyxia, the discoloration is usually an intense blue-violet or purple. In deaths by drowning, the livor mortis is light red due to contraction of small blood vessels under the skin, which is caused by immersion in cold water. In carbon monoxide poisoning, the livor mortis is cherry red, while certain poisons such as nitrobenzene or potassium chlorate impart a chocolate color to the blood.

(Continued on page A-64)

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When putrefaction commences, the blood disintegrates, and blood-stained fluid enters the tissues and body cavities by diffusion. As bacterial decomposition progresses, the livor mortis becomes dusky, then green and brown; eventually, it disappears.

Livor mortis can be distinguished from a bruise by making a cut into the area in question. Since a bruise is caused by diffusion of the blood into surrounding tissues, no blood will flow from the cut.

Rigor mortis—The stiffness that develops in the muscles after death is due to conversion of tissue chemicals to acid products. Stiffness initially develops in the muscles of the face and jaw and is first noticeable in about three to five hours after death. It then gradually involves the arms, trunk and legs, in that order. Rigor mortis is usually well developed and complete in 8 to 12 hours, and may last up to 24 hours. It then gradually passes off in the same order in which it appeared. If a person dies quietly, rigor mortis develops more slowly; conversely, if a person dies while exerting himself, it comes on more rapidly. Generally speaking, rigor mortis develops in muscular bodies more slowly and lasts for longer periods than in emaciated bodies. Heat causes rigor mortis to develop more rapidly as well as to disappear more quickly. Cold also hastens the onset of rigor mortis but causes it to remain for a longer period.

If a body is chilled or submerged after death, goose flesh of the skin may develop and persist. Cadaveric spasm may resemble instantaneous rigor mortis, but many authors claim that the two are not related. After rigor mortis is well developed and complete, it can be broken by the use of extreme force and then will not return. Embalming with fluids such as FORMALIN® will stiffen the body and produce a result similar to rigor mortis.

Postmortem eye changes—The cornea is glistening and moist during life, but it becomes dry and cloudy after death. If the eyes are open for any length of time after death, the exposed scleras may turn red-brown from drying. The pupils of the eyes may become irregular or unequal in size due to rigor mortis of the internal muscles of the eye.

Postmortem Decomposition

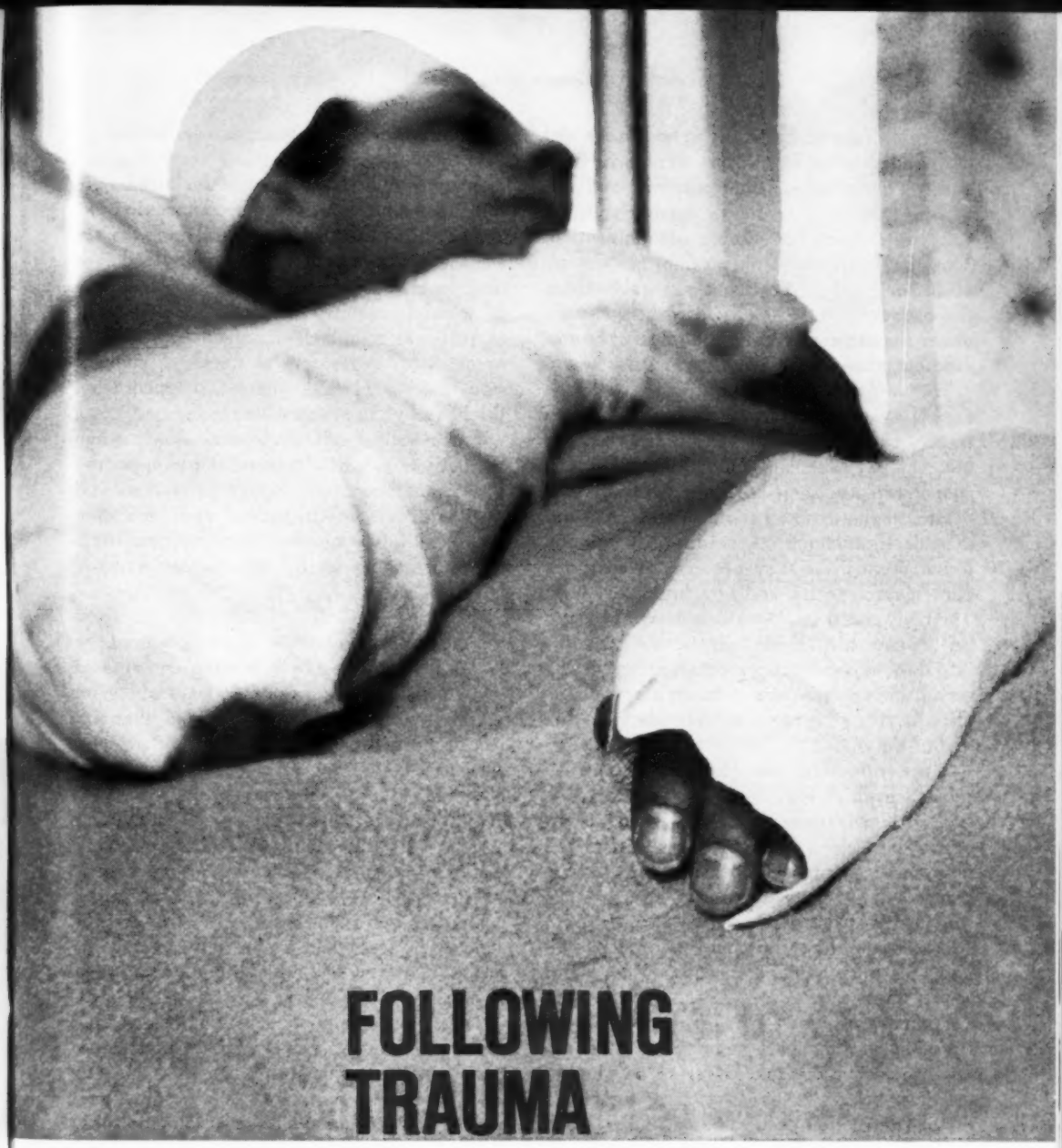
The process by which the body destroys itself may take the form of putrefaction, mummification or adipocere.

Putrefaction—When putrefactive bacteria get into the blood vessels either by way of the intestinal tract or, less often, through a skin wound, putrefaction occurs. The bacteria spread through the blood vessels and use the products of the blood as culture media. Gas-forming bacteria may invade the body soon after death or several days later. They dissolve the blood, liquefy blood clots, disintegrate tissues, and produce gas in blood vessels and tissue spaces. A common sign of bacterial decomposition is a dark green discoloration over the abdomen, appearing in 24 to 48 hours after death. This is caused by chemicals in the large intestine acting on blood. Gas bubbles may be produced in solid internal organs and in blood vessels, and gas blebs can be produced in the inner lining of the stomach and intestines. Changes in the blood produce an external effect known as marbleization.

The final result of bacterial decomposition is destruction of the body. In late stages, the organs are markedly discolored. If enough moisture is present, the organs are converted into soft, mushy masses. The body fat breaks down and becomes rancid and liquid. The bones are preserved the longest, and the skeleton and teeth may endure for years, especially if buried. Changes may vary, depending on whether the body is exposed to air, floats in water, or is buried in earth. Generally speaking, however, common phenomena occur, such as bloating and discoloration of the skin and internal membranes. Blisters which can rupture appear in the skin. Hair and nails can be pulled easily from the body. Eventually, the gases escape and the bloating subsides.

A nude body decomposes more rapidly than a protected one, because the gases can expand more readily, thus permitting rapid spread of bacteria. Mutilated bodies also decompose quickly, because external wounds allow bac-

(Continued on page A-66)



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terial putrefaction, especially in bodies drained of blood. Bodies of persons who have been poorly nourished cool more rapidly, and this retards putrefaction. Gas is less likely to develop in a body undergoing mummification. Time of death based on postmortem decomposition is only a good guess, as sometimes two or more bodies undergoing decomposition under the same external conditions will show different stages of the same process.

Mummification—A cadaver dries or shrivels due to evaporation of water. Mummification usually occurs when the body is situated in a hot, dry environment, such as a desert, or a cool dry place, such as a cemetery vault. It begins in the exposed parts of the body and extends throughout the entire body and internal organs. As they become affected, the parts shrivel, shrink and turn brown to black. The body contracts, loses weight, and becomes brittle and stiff. Eventually, it will crumple into dust; however, if protected, it can be preserved for years. Mummification may be complete in 1 to 12 months, depending on the size of the body.

Adipocere—The soaplike, rancid, greasy substance which may form during decomposition of dead tissue is called adipocere. It occurs because a body has been submerged in water or damp soil for such a long time that it loses its protecting skin. This substance will float in water. In an adult it takes from 12 to 18 months to be complete, and in full-term, newborn babies it is complete in about six to seven weeks.

Later destruction—The processes of destruction continue until the body is obliterated. The time which this takes depends on whether the body decays in air or water or under the earth. Destruction occurs most rapidly in air. It has been said that one week in air equals two weeks in water or eight weeks in soil.

Air—Decomposition in air is caused by bacterial invasion or mummification, or both. Combinations of putrefaction and mummification occur when there is bacterial invasion. The spread is slow. In the air, postmortem ravages by animals or insects hasten the process. In warm weather blowfly eggs are deposited around openings in the body. In 8 to 14 hours the eggs become larvae, which eat into the flesh.

Water—A body submerged for any length of time in water undergoes decomposition, becomes distended with gas, and floats to the surface. After a time, the skin of the hands and feet becomes swollen, wrinkled and bleached (washerwoman effect), and later it may be easily pulled off, much like a glove or stocking. After several weeks of submersion, macerated flesh can be stripped from the body by the action of currents, etc.

Earth—Disintegration occurs slowly when the body is in earth, because the temperature is low and the body usually is clothed and undisturbed. Combinations of mummification and bacterial decomposition occur, and there may be ravages by fly and beetle larvae.

Preservation of the Body

Embalming is the best way to preserve the body. This is done by removing contents of the stomach, intestines, bladder and blood vessels by trocar and suction, and then injecting Formalin-type solutions into the blood vessels. The tissues then become firm and bleached.

Unfortunately, the process of embalming stiffens the entire body and obscures many pathologic conditions. Many poisons cannot be detected after embalming. Embalming achieves best results if done as soon as possible after death and if the body is well injected. However, if the body is put in a grave it will eventually mummify and disintegrate in spite of embalming. Freezing soon after death will preserve a body for decades; however, it will decompose rapidly after thawing out. Immersion in salt wells also may preserve a body for many decades. Some poisons, such as arsenic and zinc, retard bacteria and inhibit decomposition. Bogs in many European countries contain antiseptic substances that may preserve a body for periods of up to a century.

Estimating the Postmortem Interval

Caution should be employed in estimating the postmortem interval. It is not always possible to tell with certainty the postmortem

nterval from examination of the body. The cene of death can give important clues. For xample, clues may be obtained from dates n mail or newspapers, state of food on tables, nd the number of milk bottles or newspapers n the doorstep. The condition of the ground nd clothing and sometimes the type of in-ects on or near a body all give invaluable clues as to the postmortem interval. Other factors discovered at autopsy also are useful. For example, an empty stomach or bowel or a bladder full of urine gives some indication of when the individual died. However, if a person sustains a severe brain concussion, undigested food may be found in the stomach after a 24 hour period of coma. Contrary to the old wives' tale, the hair and nails do not grow after death. They only appear to do so because the skin and scalp shrink, starting about 24 hours after death.

In conclusion, in order to provide truthful facts for the administration of justice, all criteria must be carefully weighed and evaluated before any final decision is made in estimating the time of death.

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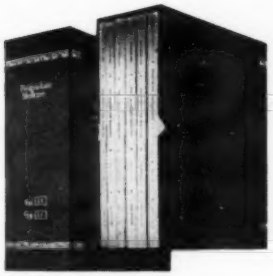

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The drug should be used with caution and in reduced dosage in patients with impaired renal function to avoid excessively high blood levels. Evidence of renal irritation frequently occurs during therapy, but this effect appears to be reversible on cessation of therapy and is not an indication for withdrawing the drug if the patient's infection is responding.

No blood dyscrasias or hepatic toxicity have been noted.

Recommended directions for the use of KANTREX Injection are contained in the Official Package Circular which accompanies each vial.

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Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations:

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume.

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1. Council on Drugs: J.A.M.A. 172:699, 1960.

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KANTREX											●	●		●	●	●	●							●			
TETREX	●		●	●	●	●	●	●	●		●	●	●		●	●	●	●	●	●	●		●	●	●	●	
SYNCILLIN																					●			●	●	●	●
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*recommended for those staphylococci resistant to other penicillins

Medicine from Abroad

FROM POSTGRADUATE MEDICINE'S CORRESPONDENTS

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AUSTRALIA: GRAYTON BROWN, M.D.
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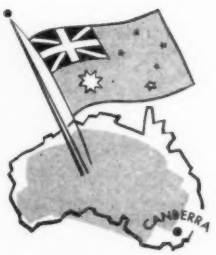
AUSTRALIA



Survival from carcinoma of the esophagus—In the *Australian and New Zealand Journal of Surgery*, Dr. E. E. Dunlop has reported on the survival of 170 patients treated at the Royal Melbourne Hospital, Melbourne, for carcinoma of the esophagus. The sites of the tumor and the sex incidence, tabulated according to the average age of the patients, and the sites of metastases were analyzed.

Palliative measures used included intubation, gastrostomy or jejunostomy, short circuits, resection and deep x-ray therapy. Major surgical excision was carried out in 116 patients (68 per cent); the operative mortality was 33 (28 per cent). There were 20 patients who survived three years and 18 who survived five years or more; of the latter, 14 were still alive from 5 to 10 years after resection.

Dr. Dunlop believes that the site of the growth should determine the operative approach. Tumors in the lower third of the esophagus were approached through a left thoracoabdominal incision; those in the middle third, through separate abdominal and right thoracic incisions. Resection of the upper third of the esophagus usually required pharyngoesophageal laryngectomy, with buried skin-tube reconstruction for those patients with a good prognosis and a split-skin graft bearing plastic tube replacement for those with a doubtful prognosis.

Coronary angiography—Drs. Graeme Sloman and W. S. C. Hare, departments of cardiology and radiology, Royal Melbourne Hospital, have reported on the clinical application of coronary angiography. Their findings have been published in the *Medical Journal of Australia*.

Increasing interest in the possibility of surgical treatment of coronary artery disease has served as a stimulus to demonstrate obstructive lesions in coronary arteries. Because clinical examinations and electrocardiograms frequently do not establish a firm diagnosis in patients with anterior chest pain, an accurate demonstration of the coronary arteries would assist in managing patients for whom a definite diagnosis is imperative. In 1948, Jonssön performed aortography, using a cardiac catheter passed through a peripheral artery into the ascending aorta to demonstrate the coronary arteries. As a part of

(Continued on page A-86)

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their clinical assessment, Drs. Sloman and Hare have performed thoracic aortography on 20 patients under local anesthesia, using 76 per cent UROGRAFIN® as the contrast medium.

In 14 patients, the ascending aorta was catheterized via the right brachial artery. In the remaining six patients, the percutaneous technic described by Seldinger was used to catheterize the ascending aorta via a femoral artery. A Siemens mobile 5 in. image intensifier was used for positioning the catheter. The electrocardiogram was monitored continuously on a cathode-ray oscilloscope, with a pressure record made as required.

No arrhythmias occurred, nor were the patients troubled to any extent by the subjective sensation of warmth or by anterior chest pain associated with the injection of a contrast medium. Technically satisfactory angiograms were obtained in 12 of the 20 patients in this series.

In the surgical treatment of such patients, angiography may aid in deciding the type of operation required and whether or not a direct approach is possible; this technic may also be of value in assessing postoperative results.

BRAZIL

Anaphylactoid purpura—N. Belliboni has reported on three cases of anaphylactoid purpura (Henoch-Schönlein purpura). He prefers the term "Henoch-Schönlein purpura" because, even though the syndrome presents varying degrees of symptomatology, it is not necessary to differentiate the distinct diseases such as rheumatic purpura and abdominal purpura.

The clinical picture in the three patients studied showed purpura without any hematologic involvement or renal lesions; however, abdominal pain of mild to severe intensity was present. The cutaneous lesions were those of common purpura associated with urticarial exanthema; some of them were characteristic of the lesions of angioneurotic edema, and others resembled erythema multiforme. Focal sepsis was found in all three patients.

Treatment consisted of administering prednisone or rutin plus vitamin C, with concomitant treatment of the focal infection. This therapy gave marked improvement and subsequent cure.

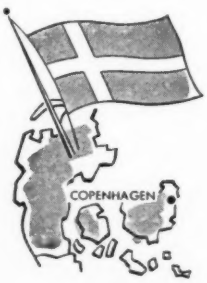
Drainage of the duct of Wirsung—P. Bove, M. R. Oliveira, P. D. Branco and S. G. de Faria have presented the results of a study of 44 patients with biliary and pancreatic disorders who were treated by *papilotomia* and catheterization of the pancreatic duct. Cholecystectomy, choledocholithotomy or plastic surgery of the common bile duct also was performed on these patients.

The pancreatic secretion was studied in 38 patients with regard to daily variations in volume and its effect on the different symptoms. Various drugs were used to determine the variations in volume, pressure, and the amylase and sodium bicarbonate content of the pancreatic secretion. By using a contrast medium in roentgenographic examination, normal and pathologic conditions of the pancreatic canalicular system were determined in 42 patients who had a drainage tube in the pancreas.

Treatment resulted in cure in 40 patients; two patients had amelioration of symptoms, one patient became worse, and one patient died.

These reports are based on articles which have appeared in *Revista do Hospital das clinicas da Faculdade de medicina da Universidade de São Paulo.*

DENMARK



Fetal mortality—During the last few years, studies have been conducted to determine why the decrease in perinatal mortality has not kept pace with the general decrease in infant mortality. The complex problems involved complicate comparisons between different studies in this field. In the *Danish Medical Bulletin*, Karen Dreyer and Svend Nørregaard have presented results of a study demonstrating a lack of sufficient information on death certificates in late fetal deaths.

The authors investigated 3,922 fetal deaths which occurred during the three year period 1955 through 1957. They classified their data according to sex, cause of death, and time of death.

(Continued on page A-88)

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formerly Natalins Comprehensive

Only one Natalins tablet per day provides generous amounts of iron, calcium, and vitamin C, plus 8 other important vitamins. This special formula helps assure, in multiparas, the extra nutritional protection they—particularly*—need. It naturally follows that this formulation will be adequate for the primigravida as well. With their new smooth coating, Natalins tablets are easier to swallow... and they disintegrate rapidly and fully for maximum utilization.

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*Traylor, J. B., and Torpin, R.: Am. J. Obst. & Gynec. 61:71-74 (Jan.) 1951.

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The time of death was unknown in about 25 per cent of cases, but the figures indicated that these deaths probably occurred during delivery, and the tables were revised accordingly. Even after this revision, the statistics showed a smaller number of deaths during delivery than was shown in a study conducted by Kærn.

Classification according to sex and cause of death showed a greater number of male infants than of female infants in most groups. However, the preponderance of cases of anencephalia in female infants accounted for a lower percentage (40.5 per cent) of deaths due to congenital malformations in male infants. Seventeen per cent of the deaths were due to ill-defined or unspecified causes. Birth injury, congenital malformations, and erythroblastosis foetalis accounted for 15 per cent of all late fetal deaths. This was the same proportion that Kærn found among perinatal deaths; however, certain predisposing factors were responsible for a greater number of late fetal deaths than of perinatal deaths.

Using figures published by the World Health Organization, the authors reviewed the causes of late fetal deaths in Denmark and in certain other countries. Denmark had the highest proportion of cases (one-third) in which death was due to ill-defined or unspecified causes, including maceration. This indicates that Danish death certificates for late fetal deaths must be improved and that the doctor's attitude toward this problem must be changed.

ENGLAND

Hazards of radiation—The Medical Research Council recently published a second report on the hazards to man of nuclear and allied radiations. The report indicates that although a great deal of new information is available there are still many gaps in knowledge of the effects of radiation, and further intensive research is still necessary. The report emphasizes the difficulty of assessing the significance of radiation in absolute terms, and instead makes use of the dose of radiation received from natural background as a reference level. In England the average dose is about 100 millirads per year. By comparison, the doses received from both the increased use of radiation in modern life and the radioactive fall-out are very small.

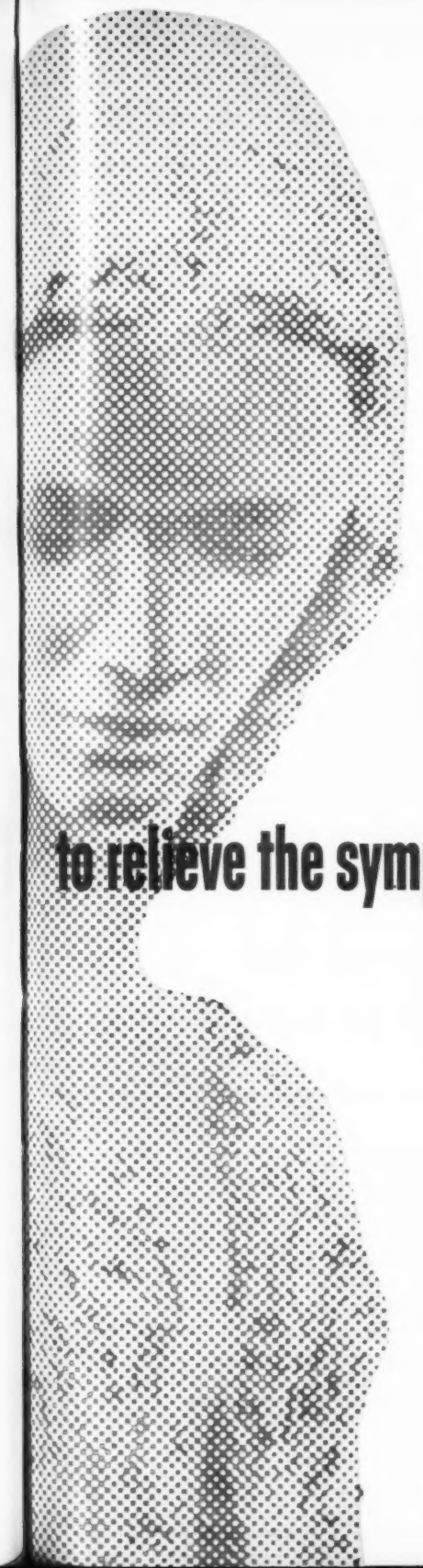
The evidence was reviewed on the possibility that roentgenographic examination of the pregnant woman's abdomen or pelvis may add to the small natural chance that leukemia might develop in her child during the early years of his life. Results of the earlier studies of the leukemogenic effect of irradiation in utero have not been substantiated by subsequent extensive investigations. However, the possibility that a small risk exists has not been disproved, and it would therefore seem prudent to reduce roentgenographic examination of the pregnant woman's abdomen and pelvis to the lowest practicable level.

With increased knowledge of the factors which determine the levels of strontium 90 in newly formed bone, the Medical Research Council does not now think that bone concentrations of this isotope would continue to rise considerably after a decrease or cessation of weapon testing. Nevertheless, since they cannot at present determine all additional sources which contribute to the irradiation of bone or bone marrow, they still think it wise to adopt a cautious attitude. They recommend, therefore, that if the concentration of strontium 90 in bone, calculated as an average for any age group, including infants and young children, was found to be rising continuously and to have reached the level of one-half of that recommended as the maximal permissible level for the population as a whole a reassessment of the situation would be required.

Lysergic acid in psychotherapy—One of the main problems in psychiatry is the time involved in psychotherapy. However, recent experience has shown that lysergic acid (LSD) in small doses can expedite this procedure. LSD is chemically related to ergot. Taken in small doses, it effects a state of reverie with a re-experiencing of memories even back to birth, accompanied by a most therapeutic abreaction. It apparently can be used safely on an outpatient basis in suitable instances.

During a discussion at the Royal Society of Medicine, Drs. T. M. Ling and J. Buckman, London psychiatrists, reported on their experience with LSD in treating outpatients. They use the following therapeutic regimen. The patients enter the hospital at 6 P.M. once a week and stay overnight. They are permitted to go to work the next morning but are advised not to drive a car until midday. In addition to receiving LSD, the pa-

(Continued on page A-90)



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DOSAGE: **Usual adult dosage is one tablet once or twice a day, beginning on the first morning of symptoms and continuing until the onset of menses. CYCLEX may be continued through the menstrual period.**

Before prescribing or administering CYCLEX, the physician should consult detailed information on use accompanying package or available on request.

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MSD

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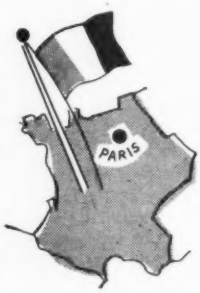
tients have at least one interview each week.

LSD is started with a dose of 40 μg. given intramuscularly together with 5 to 10 mg. METHEDRINE®, which potentiates the action of LSD and lessens anxiety. At subsequent treatments, the dose of LSD is increased by 20 μg. (These workers found the average dose to be 100 μg. LSD and 15 mg. Methedrine.) Anxious patients are started on 25 μg.; very resistant patients may need about 200 μg. The effect of the injection begins after about 15 minutes, and treatment is interrupted after four to six hours with 50 mg. MELLARIL® or LARGACTIL® given orally. After eight treatments, therapy is discontinued for a month, as LSD is cumulative.

Fifty patients who received this treatment were seen not less than six months after treatment was completed. Seven had recovered, eight were greatly improved, 23 were moderately improved, 11 were not improved, and one was worse.

FRANCE



Bone-marrow grafting—An unsuccessful attempt to treat acute leukemia by irradiation and grafts of bone marrow has been reported by G. Mathé and coworkers in *Revue d'hématologie*. The study was done on three boys, aged 6, 7 and 11 years, respectively.

Because injections of bone marrow are poorly tolerated when numerous leukocytes are circulating in the blood, the study was made when the leukemia was in remission. The patients were being treated with blood transfusions and a combination of deltacortisone and mercaptopurine. Two of them had had two previous remissions, and the third had had a single remission. At the time of the study, new remissions had just started.

The patients were irradiated with radiocobalt. Their eyes and testicles were covered, and they received 950 rads over the whole body in two sessions at 24 hour intervals. The abdomen, which was shielded for part of the time, did not receive more than 800 rads; above this limit the intestinal reactions become very painful.

The marrow became totally aplastic after the eighth day. The patients' hair started to fall out, and they became completely bald toward the fifteenth day. The graft consisted of injections totaling 400 to 600 ml. of bone marrow. The bone marrow was obtained by about 60 punctures, which were directed toward different bone segments and which yielded 5 to 10 ml. each of marrow mixed with blood (about 100 billion nucleated cells). Two of the children received maternal marrow; the third received a mixture of marrow taken from three women. Daily injections of blood platelets also were given.

The graft was a complete failure in one patient: he received an injection on June 8, 1959, and died without marrow on July 10. In the other two patients, the graft took. Myeloid recovery occurred, and leukocytes with female nuclear prolongations (proving that they had come from the blood of female donors) were present. However, a secondary syndrome, including fever, generalized erythematous rash, difficult breathing, diarrhea, vomiting, somnolence and finally coma, developed, and the patients died on the fortieth and thirtieth days, respectively, after irradiation.

Postmortem examination revealed acute edema of the lungs, with fungous infection in one patient and with a virus pneumonia in the other. (Patients with acute leukemia are very sensitive to such secondary infections, even without irradiation.) Autopsy also showed gross inflammatory lesions in the brain, liver and spleen and foci of hepatic necrosis. Hyperacanthosis, follicular dyskeratosis and metaplasia of the excretory canals of the sweat glands were observed, and complete lymphoid aplasia was present. The cause of death appeared to be a secondary syndrome due to hepatic failure and lymphoid aplasia, with fungous or viral proliferation which infiltrated several organs, particularly the lungs.

GREECE

Agenesis of the gallbladder and cystic duct—Associate Professor N. Yannopoulos, head, First Surgical Clinic, Evangelismos Hospital, Athens, and Dr. C. Pappis have reported on two cases of agenesis of the gallbladder and the cystic duct in which the biliary tract was otherwise apparently normal.

(Continued on page A-92)

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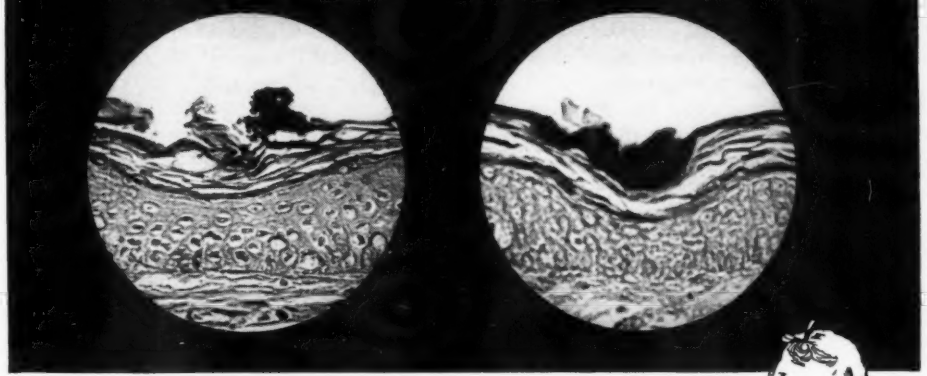

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1. Spoor, H. J.: New York St. J. M. 60:2863, 1960.
2. Wiese, H. F., et al.: J. Nutrition 66:345, 1958.
3. Smith, L. W., et al.: Amer. J. Med. Sc. 237:600, 1959.
4. Nutrition Reviews 17:136, 1959.

The first case was a 65 year old man who had surgery after a diagnosis of choledocholithiasis and jaundice. The common bile duct was dilated but there were no gallstones, and a Kehr tube drainage was performed. A retrograde cholangiogram made 14 days after the operation did not show any malposition of the gallbladder. Agenesis of the gallbladder and cystic duct also was found in a 41 year old woman. The common bile duct was normal at operation and no Kehr tube drainage was done. Both patients recovered with no complications.

After an exhaustive search of international literature, the authors revealed that 172 cases of agenesis of the gallbladder and cystic duct had been reported since 1701. The two cases which they reported bring the present total to 174.

The authors reviewed the embryonal development of the hepatobiliary tree in order to clarify the obscure etiology of this disorder.

Anticoagulant therapy—Dr. Miltiades D. Samartzis, research fellow in medicine (cardiovascular diseases), New York Hospital and Cornell University Medical College, New York, has reported on long-term anticoagulant therapy for thromboembolic complications of cardiovascular diseases.

Dr. Samartzis stated that long-term anticoagulant therapy significantly decreases the morbidity and mortality of many cardiovascular diseases by markedly reducing the recurrence of thromboembolic episodes. Prophylactic anticoagulant treatment has produced very satisfactory results and is indicated in repeated, complicated or severe myocardial infarcts; repeated cerebral thromboses and embolisms and transient cerebral ischemia attacks; repeated arterial embolisms from rheumatic or arteriosclerotic heart disease, with or without auricular fibrillation; and recurrent thrombophlebitis with pulmonary embolism. Long-term anticoagulant therapy is also recommended in the treatment of severe, progressive angina pectoris, chronic congestive heart failure, and repeated thromboembolic phenomena or progressive thrombosis elsewhere in the vascular tree. Dr. Samartzis stated that this therapy should not be undertaken unless the physician is experienced, the patient is cooperative, and services of a reliable laboratory are available.

Treatment should be started with heparin or TROMEXAN® and continued with orally administered hypoprothrombinemic drugs (DICUMAROL®, COUMADIN®, phenylindanedione or MARCOUMAR®). Quick's one-stage prothrombin time, performed on an average of every second week, provides sufficient laboratory control (therapeutic range of 25 to 35 seconds). Dr. Samartzis believes this test is preferable to Owren's prothrombin-proconvertin method (therapeutic range of 10 to 30 per cent).

If it is necessary to interrupt the therapy, dosage should be decreased gradually in order to avoid thromboembolic rebound phenomena. Treatment may be continued during operative procedures or up to the last days of pregnancy without danger to the patient, but it must be controlled at a low level. If this measure is observed, the risk of minor hemorrhagic complications is small. Vitamin K_1 has been given successfully in the rare event of severe hemorrhage.

These reports were taken from the *Evangelismos Hospital Review*.

ISRAEL

Malaria—In 1948, 1,172 new cases of malaria were reported in Israel. Since that time, the incidence of this disease has been decreasing; only 29 new cases were reported in 1958. However, in *Briuth Hatsibur*, Dr. Z. Salternick, chief malariologist of the Ministry of Health, has described a small outbreak of tertian malaria in the coastal plain. Although this region has been virtually free from malaria, in 1959 there were 21 cases, most of them occurring during August, September and October.

Field investigations showed that the *Anopheles pharoensis* mosquitoes, which are rarely seen in Israel, were breeding extensively in small pools formed by leaky water pipes. In addition, high winds during August were thought to have carried these mosquitoes to the coastal plain. It is of interest that the World Health Organization reported a sharp rise in the incidence of malaria in the neighboring Gaza region during 1959.

Thalassemia minor—Up to the present time, thalassemia minor has been observed only in Jews of the Kurdish, Iraqi and Bukharan (Central Asian) communities. However, M. Djaldetti

(Continued on page A-94)

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1. Cornely, D. A., and Ritter, J. A.: N-acetyl-p-aminophenol (Tylenol Elixir) as a Pediatric Antipyretic-Analgesic, J.A.M.A. *160*:1219 (Apr. 7) 1956.
2. Mintz, A. A.: Management of the Febrile Child, J. Ky. Acad. Gen. Pract. *5*:26 (Jan.) 1959.

and C. Klibanski, Beilinson Hospital, Petah Tiqva, have reported in *Harefuah* on the first case of thalassemia minor in a Yemenite Jew. This patient had slight hypochromic anemia, with target cells in the blood smear. Paper electrophoresis showed an increased fraction of A_2 hemoglobin (17.3 per cent); the osmotic fragility was decreased.

Amaurosis following severe hemorrhage —In *Harefuah*, E. Sinai, W. N. Wolff and M. Hirschprung have described two unusual cases of failure of vision following severe hemorrhage.

The first patient, a 41 year old man, had severe melena and hematemesis, which resulted in shock and an impalpable pulse; the red blood cell count decreased to 1,350,000. Five days following recovery, the patient became blind in the right eye. Ophthalmoscopy showed a picture typical of occlusion of the central artery of the retina. The blindness was permanent, with subsequent development of atrophy of the optic nerve.

The second patient, a 35 year old man, had severe gastrointestinal bleeding; the blood pressure fell to 90/60, and the red blood cell count decreased to 1,900,000. A week later he complained of blurred vision in both eyes. Ophthalmoscopy showed optic neuritis, with edema and hemorrhages in the retina.

The authors suggested that the fall in blood pressure and the reduction in blood volume may have caused thrombosis of the central artery of the retina, which resulted in complete occlusion in the first patient and partial occlusion in the second.

SPAIN

Award for medical research—Dr. José Luis Rodríguez-Candela, Director of the Gregorio Marañón Institute of the Superior Council of Scientific Investigations, has recently been awarded the 500,000 peseta grant for medical research from the Juan March Foundation. He received this award for his research on the mechanism of the action of insulin.

Dr. Rodríguez has devoted his entire time to medical research for many years. Born in Madrid in 1906, he was graduated from the Universidad Central de España Facultad de Medicina, Madrid, in 1931. He obtained his doctorate in 1934, writing his dissertation on the influence of the pancreas in metabolism of calcium and phosphorus. Before receiving the Juan March Foundation grant, Dr. Rodríguez held the chair of general pathology in the Universidad Literaria de Valladolid Facultad de Medicina for 20 years. He then became director of the Metabolic Institute of the Superior Council of Scientific Investigations, and later was appointed director of the institute created in memory of Dr. Gregorio Marañón. Dr. Rodríguez has published two books, one on clinical exploration and one on medical research. He reads and speaks French, English and German and has published many articles in local and foreign scientific journals. He also has lectured abroad at various scientific congresses.

In commenting on his grant, Dr. Rodríguez stated that for the past eight years he has been investigating the mechanism of the action of insulin. This hormone is being studied in many countries, and Dr. Rodríguez expects to attend an international congress on insulin in July 1961.

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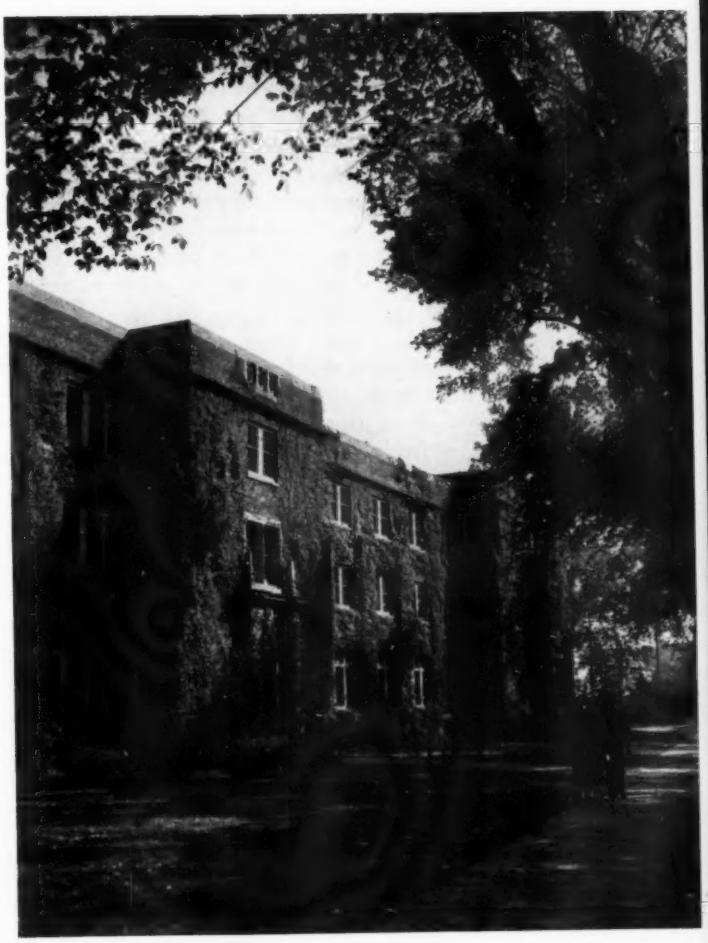

A special series
adapted from a course
presented at the
University of Minnesota
Center for Continuation Study

Part 1

INTRODUCTION

In the most general terms, one can say that the acquisition of information is part of the process of obtaining an education. This is a dynamic process, as information is made up of facts which are modified and amplified by newer developments. As a result we must keep abreast of new facts if we are to continue our education and remain up to date.

In no profession is the necessity to continue one's education so important as in medicine. Each day there are advances which lead to improvement in the care the physician can provide for his patients. The physician who does not keep up with these advances, or who is unaware of the changes in the techniques of his profession, is in the tragic position of being shoved into mediocrity, much as the workman whose job is made obsolete by technological advances.

The physician can continue his education in many ways: by reading the current literature, by discussions with his associates, or by attending courses at various medical centers in which other physicians in more specialized segments of medicine can share some of the newer ideas and concepts with which they are working.

The series of articles which follows and which will be completed in the April and June issues of this Journal represents the last-named type of continuing education. These papers have been adapted from lectures given during a Continuation Course in Emergency Surgery offered by the Department of Surgery of the University of Minnesota Medical School. Some of the ideas expressed here are new; some have been established for a considerable time; but all of the authors share the belief that to be a good physician and to give the best possible care to the largest number of patients, a physician must know *why* a disease is treated in a particular manner, rather than simply *how* a disease or injury is treated.

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Abdominal Injuries

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I WOULD like to discuss some of the aspects of abdominal injury considered to be important to proper treatment. These injuries are increasing in frequency, primarily because of the increasing incidence of automobile and pedestrian accidents. We hear a great deal about fatalities from automobile accidents but relatively little about nonfatal accidents and the people who have injuries that are less than lethal and who survive to be treated. Yet it is this group that is important to the physician, since it affords an opportunity to save a life and to restore the injured to health.

OSCAR CREECH, JR.

Specifically, I wish to make some remarks regarding the mechanisms of abdominal injury, the pathologic changes resulting from injury, the clinical manifestations, the important features leading to a correct diagnosis, and, finally, the treatment. With regard to treatment, it should be emphasized that once the diagnosis has been established and the patient properly resuscitated, treatment of specific intraabdominal injuries follows established surgical principles.

My remarks are based primarily on a large experience with abdominal injuries at the Charity Hospital in New Orleans. We not only have our share of irresponsible drivers, but unfortunately we also have people who engage in other types of irresponsible activity with lethal or semilethal weapons. Thus we encounter abdominal trauma in many forms.

Mechanisms of Abdominal Injury

Penetrating wounds are most often a result of ice picks and knives, firearms, flying objects and impalement (figure 1). Among these, ice picks and knives are the most frequently encountered devices. Of wounds resulting from firearms, the most common are those due to pistol shot; injury resulting from

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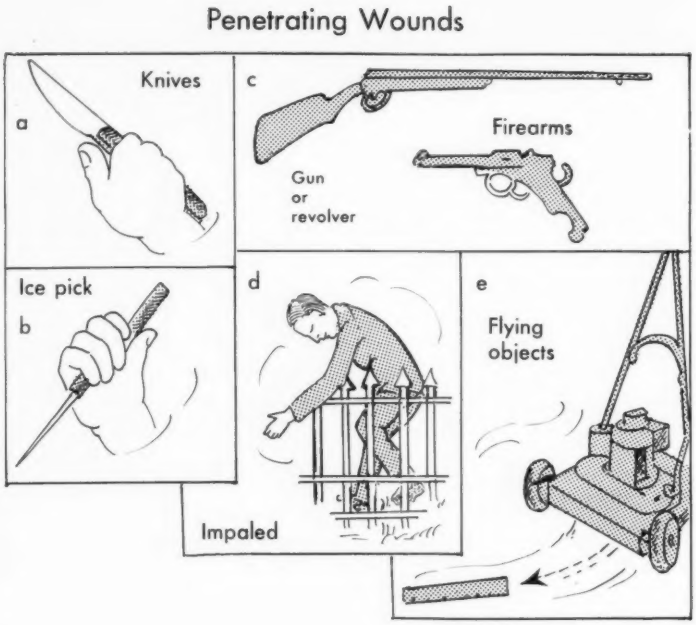

FIGURE 1. Common causes of penetrating wounds of the abdomen.

rifle fire is extremely uncommon. Wounds due to flying objects are a result of the rotary power mower in most instances. Either a blade of the mower or a piece of stone or metal propelled by the rotary blade is responsible.

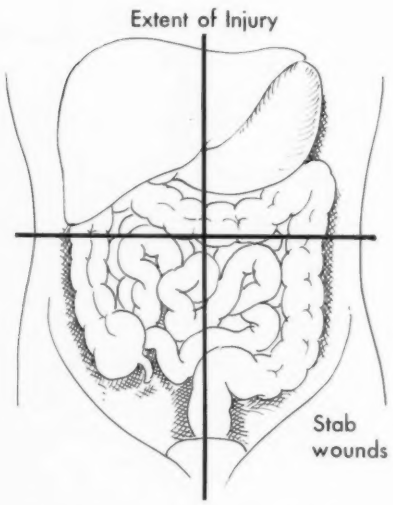

FIGURE 2. An abdominal injury resulting from a stab wound usually is confined to the quadrant in which the external wound is located.

The extent of injury following a penetrating wound can be deduced to a considerable extent from the knowledge of the type of injuring agent. For instance, when a stab wound occurs the intraabdominal injury usually is confined to the abdominal quadrant in which the external wound is located (figure 2). To be sure, a "switch blade artist" may insert a knife into his victim and sweep the blade in a 90 to 100 degree arc, thus producing damage to structures in more than one abdominal quadrant. However, this is an exception. If a wound is due to a high-velocity missile, the tract of the missile usually is such that it involves more than one abdominal area and multiple visceral injuries result (figure 3). The course the missile takes is not always a straight line, since it may be deflected by certain tissues. Nevertheless, one can predict with reasonable accuracy the likelihood of involvement of intraabdominal structures from the location of the wounds of entrance and exit or from the location of the missile as observed on an x-ray.

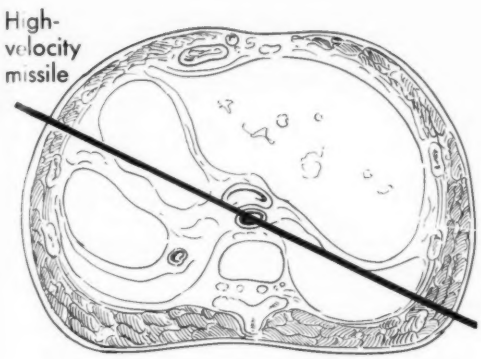

FIGURE 3. A wound due to a high-velocity missile usually involves multiple abdominal viscera. The missile's course is not always straight, but the entrance and exit wounds or the location of the missile as observed on an x-ray permits reasonably accurate prediction of structural involvement.

Shotgun wounds of the abdomen are less common than pistol-shot wounds but are encountered occasionally as a result of hunting accidents. In this type of wound the pattern of injury is diffuse with the greatest injury occurring in the center of the pattern and decreasing severity of injury as the periphery is approached. Although a shotgun wound may involve a rather extensive area on the abdominal or lower chest wall, the intraabdominal injury usually is not severe unless the shooting occurred at close range (figure 4).

It has been of interest to us to observe the seasonal and chronologic occurrence of gunshot wounds in our city. In reviewing a small series of these injuries we noted that a majority occur in the winter and between the hours of 9 o'clock in the evening and midnight (figure 5). Gunshot wounds are least frequent in the fall and between the hours of 6 and 9 o'clock in the evening. You may infer from these data what you will!

Nonpenetrating injury of the abdomen may result from automobile accidents, explosive blasts, and kicks, either by man or by animals (figure 6). With the exception of kicks, the injuring force is applied diffusely, so that one can derive but little information regarding the sites of intraabdominal injury from a knowledge of the injuring agent.

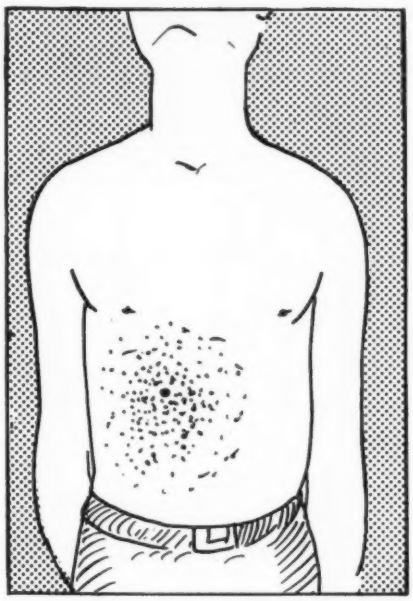

FIGURE 4. A shotgun wound produces a diffuse pattern of injury, most severe at the center and decreasing in severity toward the periphery.

Primary Effects of Injury

Irrespective of the mechanism of injury and whether the wound is penetrating or nonpenetrating, the primary effects of abdominal injury are hemorrhage and peritonitis (figure 7). It is immediately evident that these two states are interrelated, since intraabdominal hemorrhage produces peritoneal irritation as well as reduction in circulating blood volume, while peritonitis is associated with peritoneal irritation and, if severe, with reduction in circulating blood volume. Although this interrelationship may sometimes make it difficult to differentiate between hemorrhage and peritonitis as a cause of the clinical manifestations, in general the signs of reduction of blood volume which follow peritonitis will appear later than those which occur following hemorrhage.

Pathologic Anatomy

In a recent analysis of 400 cases of stab wounds of the abdomen reviewed by one of

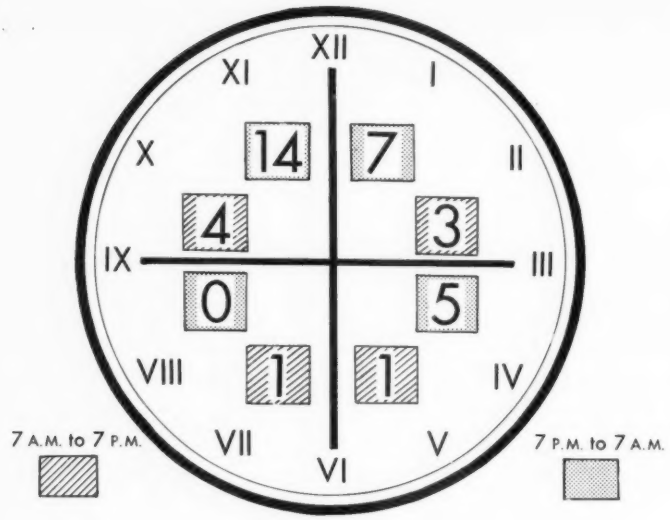

FIGURE 5. Chronologic pattern of a small series of gunshot wounds. Majority of the injuries occurred between 9 and 12 o'clock at night.

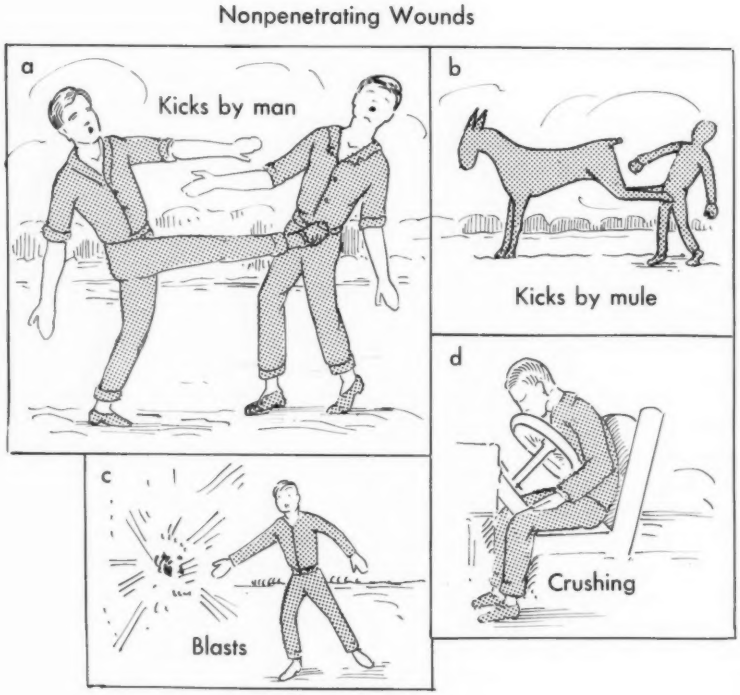

FIGURE 6. Common causes of nonpenetrating abdominal injuries.

my associates, Dr. Kenneth Moss, it was found that a variety of intraabdominal structures were injured (table 1). In about one-fourth of the cases the liver was involved, with the stomach, small intestine and large intestine next in order of frequency. Although retro-

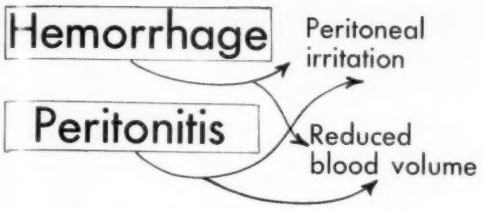

FIGURE 7. Primary effects of any abdominal injury.

peritoneal hematoma occurred in 5.75 per cent, injury to retroperitoneal viscera (duodenum, pancreas and kidney) was less common. In contrast, a review of 30 cases of gastrointestinal perforation following nonpenetrating abdominal trauma disclosed injury to the stomach in one instance, duodenal injury in two, jejunal injury in 18, injury to the ileocecal region in eight, and injury to the sigmoid in one (figure 8). The frequency with which the spleen and liver are involved in nonpenetrating abdominal trauma is well known and does not require elaboration here.

Diagnosis

Having in mind the mechanisms of injury, the frequency of involvement of the various intraabdominal structures, and the primary effects of injury, let us consider the diagnosis. It must be emphasized that one needs to rely on clinical manifestations in order to make an early correct diagnosis. History is important, to be sure, and should be carefully elicited whenever possible. Unfortunately, many of these patients are comatose or are so confused that a reliable history cannot be obtained.

TABLE 1

INCIDENCE OF INJURY TO ABDOMINAL AND THORACIC STRUCTURES IN 400 CASES OF STAB WOUNDS OF THE ABDOMEN

Liver	103
Stomach	55
Small bowel	50
Large bowel	35
Omentum	27
Spleen	26
Hematoma (retroperitoneal)	23
Diaphragm	19
Mesentery	15
Pneumothorax	14
Gallbladder	11
Bleeding wound, hemothorax	10
Inferior vena cava	8
Duodenum, pancreas, mesocolon	7
Intercostal artery	5
Kidney	4
Aorta, uterus, bladder	1

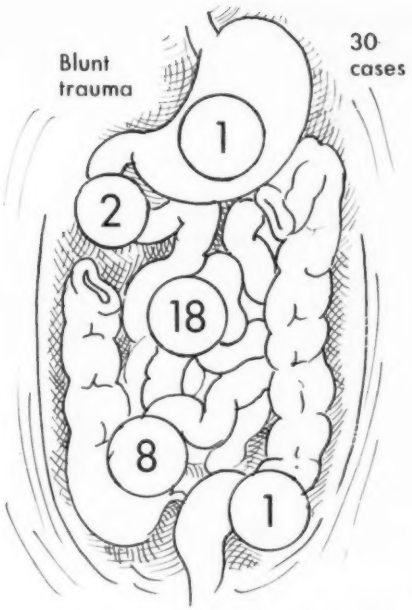

FIGURE 8. Incidence of involvement of various abdominal structures in 30 cases of gastrointestinal perforation following nonpenetrating abdominal trauma.

Signs of peritoneal irritation usually are present following injury to intraabdominal structures. Next in frequency is the evidence of intraabdominal hemorrhage. The manifestations of peritoneal irritation and intraabdominal hemorrhage often can be detected only by frequent careful examination. If the patient is examined shortly after injury, physical signs may be equivocal, but as bleeding and peritonitis continue the signs become more clear-cut and subsequent examination will reveal the presence of intraabdominal injury.

Tenderness over the abdomen is the most common finding. Then comes abdominal pain and, finally, auscultatory evidence of reduced peristalsis (figure 9). One or all of these manifestations are present in about 90 per cent of conscious patients. The next most help-

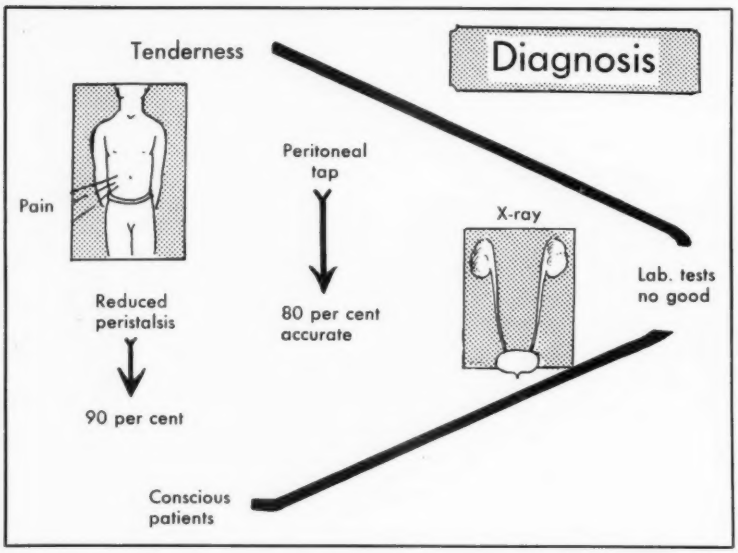

FIGURE 9. Tenderness, pain or reduced peristalsis, or a combination of these three findings, is present in about 90 per cent of conscious patients with intraabdominal injury. Paracentesis is about 80 per cent accurate in indicating hemorrhage or peritonitis. X-rays are not of much help except in detecting genitourinary injuries. Laboratory data are of even less value.

ful diagnostic maneuver is paracentesis of the abdomen, which in our experience is accurately indicative of hemorrhage or peritonitis in about 80 per cent of cases. This procedure will be described in detail later.

One should not expect to get much help from x-ray examination in establishing the diagnosis, except in instances of injury to the genitourinary tract. At best, roentgenograms of the abdomen are suggestive, but without the support of physical findings they usually are inadequate. As for laboratory examinations, these are of even less value, and aside from the detection of blood in the urine they are of little practical value.

Although roentgenograms do not often establish the correct diagnosis of other abdominal injuries, they are invaluable in detecting injury to the genitourinary tract (figure 10). Intravenous pyelograms will clearly reveal nonfunction of or extravasation from an injured kidney. The following cases illustrate the value of excretory urograms.

A child ran into a clothesline which struck him across the middle of the abdomen. When he was admitted to the hospital it was obvious that there was intraabdominal injury, and it was the consensus that the injury consisted of a ruptured spleen. However, to rule out injury to the urinary tract an intravenous pyelogram was obtained which disclosed extravasation of dye around the right kidney, although

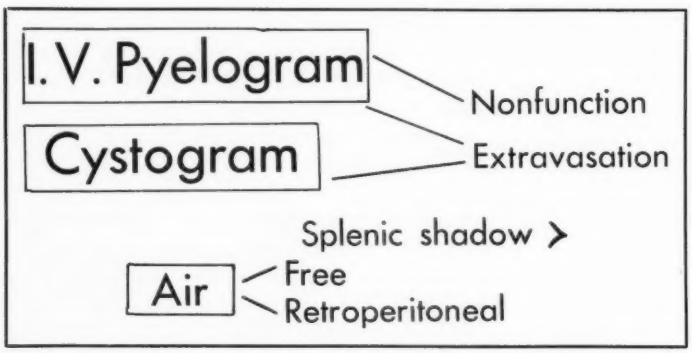

FIGURE 10. Roentgenography is invaluable in detecting injury to the genitourinary tract.

FIGURE 11. Extravasation of dye around right kidney in intravenous pyelogram of a child injured when he ran into a clothesline. There was no blood in the urine. Operation disclosed splenic rupture and complete disintegration of the right kidney.

FIGURE 12. Displacement of left ureter toward midline. Patient was kicked in the left flank. Perforation of the descending colon and a large surrounding hematoma were found at operation.

there was no blood in the urine (figure 11). At operation it was found that the spleen was ruptured, but there was also complete disintegration of the right kidney.

A man was kicked in the left flank during a barroom brawl and came to the hospital several hours later with signs of peritonitis. An intravenous pyelogram disclosed displacement of the left ureter toward the midline (figure 12). At operation there was a perforation of the descending colon with a large surrounding hematoma.

In addition to detecting rupture of the bladder, a cystogram also may aid in diagnosis of retroperitoneal hematoma prior to operation. A child was crushed between two moving automobiles, and when admitted to the hospital was in severe shock without evidence of peritonitis. A cystogram showed a pear-shaped bladder deformity indicative of an extensive retroperitoneal hematoma (figure 13).

As experience with acute traumatic conditions accumulates, it becomes evident that vascular injury is often associated with abdominal trauma. Thus, we are employing arteriography with greater frequency in an attempt to detect arterial injury prior to operation. Recently a patient was admitted to the hospital following an automobile accident. There were obvious signs of peritoneal irritation, and blood was present in the urine. An intravenous pyelogram revealed nonfunction of the left kidney, and on a lumbar aortogram the left renal artery could not be visualized (figure 14). At operation it was found that the left renal artery had been sheared off from the aorta.

FIGURE 13. A cystogram may aid in preoperative diagnosis of retroperitoneal hematoma, as this film did. The patient, a child, was crushed between two moving automobiles and was in severe shock without evidence of peritonitis. Pear-shaped deformity of bladder indicates hematoma.

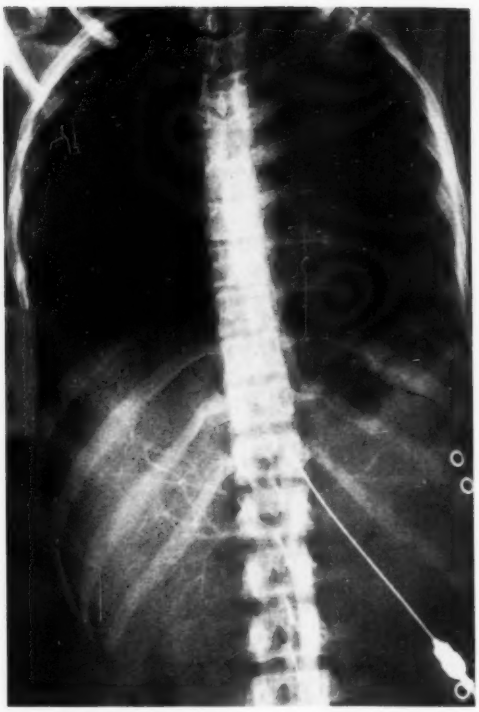

FIGURE 14. Vascular injuries are often associated with abdominal trauma, and arteriographic studies are being made with greater frequency to detect them. In this patient, who was injured in an automobile accident, the left renal artery was not visualized on a lumbar aortogram. It had been sheared off from the aorta.

Perforation of a hollow viscus as a result of abdominal trauma may produce air under the diaphragm which is detectable on the roentgenogram (figure 15). Injury of the spleen with hematoma formation may be evident from the x-ray examination. In one instance the roentgenologist was performing a barium enema study following a gastrointestinal series and observed that the stomach was displaced medially and the splenic flexure of the colon was displaced downward by a shadow in the left upper quadrant (figure 16). Careful questioning of the patient disclosed that he had sustained an insignificant blow to the left chest cage eight days previously. At operation a subcapsular hematoma of the spleen was found.

The diagnostic value of abdominal paracentesis was mentioned earlier. Because of its importance I would like to describe the technic (figure 17). For this procedure we use a Potter needle which is fluted on the end and has an opening on the side. In years past it was used in inducing artificial pneumothorax for the treatment of tuberculosis. The lower quadrants of the abdomen are prepared with antiseptic solution, and the skin and subcutaneous tissues are infiltrated with 1 per cent NOVOCAIN®. A 10 cc. syringe is attached to the Potter needle and it is inserted into the abdominal cavity through the anesthetized area. Aspiration is carried out, and if negative a second aspiration is made in a similar site in the opposite lower abdominal quadrant. Since this test is negative in about 20 per cent of cases in which there is significant

FIGURE 15. Air under the diaphragm in a case of perforation of a hollow viscus due to abdominal trauma.

abdominal injury, it should not be employed until thorough evaluation of the patient has been made. It is not a substitute for clinical judgment.

Treatment

The immediate treatment of a patient with abdominal injury should begin before examination and then proceed simultaneously with examination. While many of these patients will have multiple injuries and will require the attention of a variety of specialists, the physician to whom the patient presents himself first is the one who should decide the direction the case will take. I do not mean to imply that the physician making the initial examination will necessarily do all that needs to be done, but there are certain things he must do if the patient is to survive in a condition which will permit definitive therapy. For instance, one must insure that the patient has an adequate airway and an adequate circulating blood volume. A patient with an abdominal injury may also have an obstructed airway from tracheal or intrathoracic injury or from aspirated vomitus or from other causes. He may be comatose and the pharynx may be blocked by the tongue. Therefore, one must make certain that air is moving in and out of the lungs in adequate quantities, and that the lungs are sufficiently expanded to provide the necessary contact between alveolar air and blood in the pulmonary capillaries.

Any patient who has severe abdominal injury will have some reduction of the circulating blood volume, and this usually is evident by an increase in the pulse rate and a reduction in blood pressure. It is a policy in our emergency room to start a solution of crystalloid (physiologic saline or dextrose) solution at the time the patient is typed and cross matched for blood. We then complete the initial physical examination, and by this time blood will be available for administration if necessary. When the patient is admitted in extreme shock, a plasma expander is administered instead of a crystalloid solution.

After initial resuscitative measures have been taken, one can begin to assess the extent of total injury. One can determine the presence of major fractures, significant thoracic injury, damage to the urinary tract, and the presence of blood in the abdomen. Fractures should be properly splinted before the patient is moved for x-rays or to the operating room. The blood volume should be replaced also before the patient is moved, unless it is evident that continued massive hemorrhage is taking place. If there is associated thoracic injury with the presence of hemopneumothorax, this should be managed by insertion of an intercostal catheter connected to underwater drainage.

Illustrative Cases

To illustrate the important features in the management of abdominal injury, I would like to present briefly the chronology of treatment in several patients.

Case 1 (table 2)—A 14 year old boy was run down by an automobile and was brought

FIGURE 16. Splenic injury with hematoma may be evident from x-ray examination. This patient had a subcapsular hematoma of the spleen as a result of a seemingly insignificant blow to the chest eight days earlier.

to the emergency room within one hour. He was moderately hypotensive, and dextrose solution was started as an infusion. When blood became available, 500 ml. was administered promptly. Examination of the abdomen disclosed abrasions over the left upper quadrant and over the left lower costal margin. There was also abdominal tenderness. Fifteen minutes after admission, abdominal paracentesis was performed and yielded nonclotting blood. At operation a ruptured spleen was removed. During the operation the patient required 1500 ml. of blood to stabilize his blood pressure. This case illustrates that the severity of the deficit in blood volume due to hemorrhage may not be apparent prior to operation. However, as soon as the abdomen is opened,

TABLE 2

CASE 1: CHRONOLOGY OF EVENTS

10:30 A.M.	Patient run down by automobile
11:30 A.M.	Arrival in emergency room. Blood pressure 90/60, pulse 100
	Infusion of 300 ml. 5 per cent dextrose in physiologic saline solution
	Administration of 500 ml. blood; blood pressure 110/70
11:40 A.M.	Examination. Abrasions, left upper abdominal quadrant, lower left chest; abdominal tenderness
11:45 A.M.	Abdominal paracentesis, nonclotting blood
12:00 noon	Operation. Lacerated spleen removed. Tear in left lobe of liver repaired. Blood administered, 1500 ml.
1:00 P.M.	Operation concluded
	(Total blood administered, 2000 ml.)

TABLE 3

CASE 2: CHRONOLOGY OF EVENTS

October 11, 6:10 P.M.	Patient struck left side of chest against chair
October 16, 5:45 A.M.	Arrival in emergency room. Blood pressure 105/70, pulse 88. Sharp pain, left lower chest, left upper abdominal quadrant, left shoulder. Abdominal examination negative
6:00 A.M.	Hematocrit 23 vol. per cent
4:00 P.M.	No change in physical signs
October 17 7:00 A.M.	Abdominal paracentesis, nonclotting blood. Administration of 1500 ml. whole blood
8:00 A.M.	Operation. Subcapsular hematoma of spleen with rupture. Splenectomy. Administration of 1000 ml. of blood
9:00 A.M.	Operation concluded
	(Total blood administered, 2500 ml.)

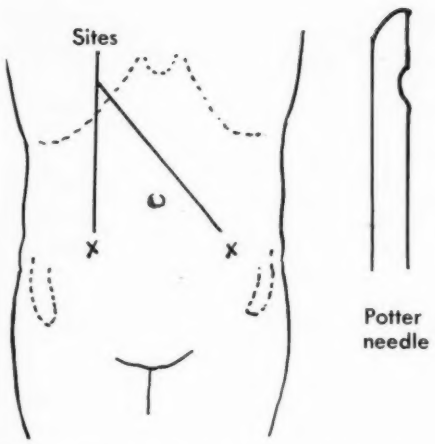

FIGURE 17. Diagram showing sites of abdominal paracentesis and Potter needle used.

the blood pressure falls and additional blood is required to stabilize the blood pressure and pulse. In this instance the blood pressure was 110/70 mm. Hg when the patient was moved to the operating room, but as soon as the abdomen was opened it fell and 1500 cc. of blood was required to restore the pressure to normal.

Case 2 (table 3)—A 23 year old woman struck the left lower portion of her chest against a chair on October 11. Although the site of injury was painful for a few moments, she subsequently forgot about it until October 15, when she began to have pain in the left lower part of her chest, left upper abdominal quadrant and left shoulder. She came to the emergency room the following morning. Examination failed to reveal significant abnormalities, although the hematocrit was 23 vol. per cent. This, combined with the symptoms, suggested splenic injury, so she was examined repeatedly by the residents. On October 17, abdominal paracentesis yielded nonclotting blood. Operation was performed and a subcapsular hematoma of the spleen was found. Splenectomy was followed by uneventful recovery. In this case 2500 ml. of whole blood was required to restore the blood volume to normal.

TABLE 4

CASE 3: CHRONOLOGY OF EVENTS

11:05 P.M.	Stab wound in abdomen
11:35 P.M.	Arrival in emergency room. Blood pressure 110/70, pulse 120. Infusion of 5 per cent dextrose in physiologic saline solution. Omentum protruding from ¾ in. wound in epigastrium. General abdominal tenderness
2:35 A.M.	Operation; 200 ml. blood in peritoneal cavity. Lacerations of anterior wall of stomach and right lobe of liver repaired
3:40 A.M.	Operation concluded
	(No blood administered)

Case 3 (table 4)—A 24 year old man received a stab wound in the abdomen and was brought to the hospital immediately. Blood pressure was normal and there was slight tachycardia. Omentum was protruding through a wound in the epigastrium. Operation was performed promptly, and a perforation of the anterior wall of the stomach and a laceration of the right lobe of the liver were repaired. The patient did not receive any blood and was discharged from the hospital within six days.

Case 4 (table 5)—A 52 year old man was found by the police some time after an auto-

TABLE 5

CASE 4: CHRONOLOGY OF EVENTS

12:30 A.M.	Arrival in emergency room. Patient found by police after automobile accident. Steering-wheel injury. No blood pressure. Dextran infusion, 1000 ml. Ventilation adequate
12:45 A.M.	Administration of 1000 ml. blood. Blood pressure 100/60
12:50 A.M.	Diminished breath sounds, right lung; general abdominal tenderness; diminished peristalsis
1:00 A.M.	Abdominal paracentesis, blood
1:05 A.M.	Right thoracentesis, hemothorax. Intercostal tube, water-sealed drainage
1:15 A.M.	Patient moved to operating room. Blood pressure became imperceptible when anesthesia started. Cardiac arrest. Thoracotomy and cardiac massage. Resuscitation
1:45 A.M.	Abdominal exploration. Ruptured spleen removed; avulsion of mesenteric root repaired; laceration of superior mesenteric vein repaired; lacerated duodenum repaired
3:00 A.M.	Operation concluded
	(Total blood administered, 6000 ml.)

TABLE 6

CASE 5: CHRONOLOGY OF EVENTS

2:00 A.M.	Arrival in emergency room, comatose, after injury in automobile collision; patient ejected from car. Blood pressure 84/40, pulse 100
2:05 A.M.	Dextran infusion. Ventilation adequate
2:20 A.M.	Blood pressure 90/50. Administration of 500 ml. blood, nasal oxygen
2:45 A.M.	Blood pressure 120/70, pulse 90. Gastric tube inserted. Urinalysis and abdominal paracentesis yielded blood
3:00 A.M.	X-rays. Fractures of left humerus, right radius, six ribs, right acetabulum
3:15 A.M.	Blood pressure 80/50, pulse 110. Administration of 500 ml. blood
3:30 A.M.	Blood pressure 100/60. Administration of 500 ml. blood
4:00 A.M.	Moved to operating room. Blood pressure (?), 1000 ml. blood
4:15 A.M.	Anesthesia. Blood pressure 90/60, 1500 ml. blood
4:20 A.M.	Operation. Repair of laceration of liver; ruptured spleen removed; compound fractures debrided; tracheostomy
6:15 A.M.	Operation concluded
	(Total blood administered, 6000 ml.)

mobile accident. He was brought to the emergency room. Blood pressure could not be detected. Dextran was administered immediately, and as soon as blood was available 1000 ml. was given rapidly, with the result that the blood pressure rose to 100/60 mm. Hg. Twenty minutes after admission, examination was begun. Breath sounds over the right side of the chest were diminished and there was generalized abdominal tenderness and reduced peristalsis. Abdominal paracentesis yielded blood, and thoracentesis on the right side revealed hemothorax. A catheter was inserted into the right side of the chest through an intercostal space and connected to water-sealed drainage. The patient was then moved to the operating room. When anesthesia was started the blood pressure became imperceptible and cardiac arrest ensued. The thorax was opened and cardiac massage was instituted, and after about 30 minutes a forceful beat was resumed. The abdomen was then opened, and the following injuries were found: rupture of the spleen, occlusion of the root of the mesentery, laceration of the third portion of the duodenum, and laceration of the superior mesenteric vein. All these structures were repaired and the spleen was removed; however, it proved necessary to administer 6000 ml. of whole blood to maintain a satisfactory blood pressure. In retrospect, it is evident that blood volume replacement had not been adequate when the patient was moved to the operating room; this caused cardiac arrest.

TABLE 7

CLASSIFICATION OF 400 CASES OF STAB WOUNDS OF ABDOMEN ACCORDING TO PENETRATION AND INJURY

GROUP	PENETRATION	INJURY
1	No	None
2	Yes	None
3	Yes	Trivial
4	Yes	Serious*

*Shock; laceration of hollow viscus, partial or complete; active hemorrhage; hemoperitoneum, 500 cc. or more.

Case 5 (table 6)—A 21 year old man was driving at high speed and ran into a bridge abutment. He was ejected from his automobile and was brought to the emergency room in a comatose state. Blood pressure was 84/40 mm. Hg, and pulse rate was 100 per minute. A dextran infusion was started while blood was being typed and cross matched. During examination of the abdomen, the blood pressure fell, and after administration of 500 ml.

TABLE 8

MORTALITY IN 400 CASES OF STAB WOUNDS OF THE ABDOMEN

GROUP	NUMBER OF CASES	DEATHS	
		Number	*Per cent*
1	73	0	
2	77	0	
3	66	0	
4	184	5*	2.7
Total	*400*	*5*	*1.3*

*Pneumonia, one; hemorrhage, four (vena caval injuries, three; aortic, one).

of blood it rose to 120/70 mm. Hg. At this time a gastric tube was inserted and urinalysis and abdominal tap were performed. There was gross blood in the urine and in the abdomen. One hour after admission, the patient was moved to the x-ray room, where fractures of the left humerus, the right radius, six ribs and the right acetabulum were demonstrated. When the patient was returned to the emergency room the blood pressure dropped to 80/50 mm. Hg, and 1000 ml. of blood was administered. In spite of continued transfusion, the pressure did not stabilize, so the patient was moved rapidly to the operating room and a celiotomy was performed. A laceration of the liver was repaired, a ruptured spleen was removed, the compound fractures were debrided, and a tracheostomy was done. During operation 6000 ml. of blood was required for replacement. Upon completion of the operation the blood pressure was 130/90 mm. Hg. The patient recovered uneventfully. This case illustrates the fact that one cannot spend too much time preparing a patient for operation when the condition for which operation is being done is rapidly destroying him. This applies not only to abdominal trauma but to injuries and disease of any kind. Thus, we must achieve a proper balance between preparation for operation and the operation itself, and considerable clinical judgment is required.

In general, it is our policy to err on the side of operation in dealing with abdominal injuries. This is particularly true in the case of penetrating wounds, since we have learned that the risk of exploration is small and the results are gratifying in terms of being able to repair damage which was not apparent clinically. In a series of stab wounds of the abdomen to which I referred earlier, it was found that a majority occurred in the anterior abdominal wall, particularly in the upper quadrants. These cases were divided into four groups according to the following criteria: (1) no intraabdominal penetration and no intraabdominal injury, (2) penetration into the abdominal cavity but no intraabdominal injury, (3) penetration into the abdominal cavity with trivial abdominal injury, and (4) penetration with serious abdominal injury (table 7). An analysis of the results in these four categories reveals that no deaths occurred in groups 1, 2 and 3 and the mortality in group 4 was only 2.7 per cent (table 8). Thus, the mortality rate for the total series (and operation was performed in each of these cases) was 1.3 per cent. I would like to add, and not without considerable pride, that these patients with stab wounds of the abdomen, and, in fact, almost all the patients I have discussed herein, were treated by our residents. As these statistics demonstrate, it was good treatment.

Management of Subphrenic Abscess

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INFECTIONS of the subphrenic space occur much more frequently than is commonly supposed, but fortunately the vast majority subside spontaneously without suppuration. Although the use of antibiotics has reduced the incidence of subphrenic abscess, it is still a frequent complication of surgical procedures. The condition is often difficult to diagnose and treat. Mistakes in management may be catastrophic for the patient. The clinical picture often is obscured by the causal condition, whether it is a ruptured appendix, a perforated ulcer or a previous operative procedure, and by the masking effect of antibiotic therapy. Moreover, few surgeons have had extensive experience with the condition, and it would seem that to be an authority on subphrenic abscess might be a rather dubious distinction.

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Definition of Subphrenic Abscess

In this discussion "subphrenic space" denotes the area from the diaphragm to the transverse colon and mesocolon. This region is divided by the liver into the suprahepatic and infrahepatic compartments. The term "subphrenic" as used to designate localization of an abscess has come to be generally accepted as referring not only to the region immediately below the diaphragm but also to an area extending as far down as the transverse colon.

Based on this more comprehensive definition, the subphrenic space is subdivided by the ligaments of the liver and adjacent structures. It is a common misconception that the liver is suspended from the dome of the diaphragm by the falciform, coronary and triangular ligaments. Actually the coronary and triangular ligaments are attached to the posterior aspect of the liver and to the posterior abdominal wall, which is the diaphragm at this level. Thus, the coronary

ligaments suspend the liver not from above but from the dorsum. Boyd[1] has recently reemphasized this anatomic relationship, and it can be confirmed at any abdominal operation or by a visit to the postmortem room. It is typical of other suspensory ligamentous relationships and may possibly be related to our four-footed origin.

Figure 1 illustrates what I have just said. In most textbooks of anatomy, the liver is depicted as being suspended from above instead of from the dorsum. It is clear that on the right side there are only two spaces, the suprahepatic and the subhepatic or infrahepatic space, separated by the liver. The so-called right posterior superior subphrenic space is a relatively descriptive terminology and is an anatomic myth. The right posterior superior intraperitoneal space actually represents the right infrahepatic space, and it is a common site of infection. In Ochsner and Graves'[2] series of 3,372 collected and personal cases about one-third of the infections were localized to this site.

On the left side a large potential space separates the diaphragm from the left lobe of the liver, the fundus of the stomach, and the spleen. Though the left lobe of the liver is related to about a half or less of the diaphragm, this space is best called the left suprahepatic space, to conform with the terminology applied to the right side. Mitchell[3] calls this space the left subphrenic space, a term which, although more accurate anatomically, is confusing in view of the wider significance of the term "subphrenic" as applied to all infections located in the region below the diaphragm.

There are two infrahepatic spaces on the left side (figure 2). The left anterior infrahepatic space, beneath the left lobe of the liver, communicates widely with the left suprahepatic space, and it is regarded by Mitchell as being merely a subhepatic extension of the suprahepatic space. The left posterior infrahepatic space comprises the lesser sac of the peritoneum itself. It extends up much higher between the liver and the diaphragm than does the right suprahepatic space.

Thus, on the right side the subphrenic space

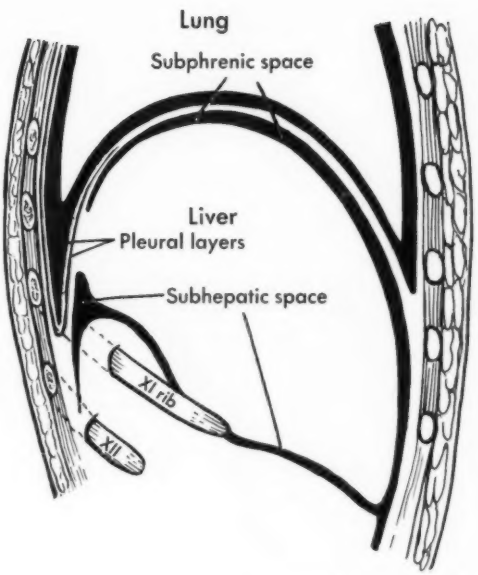

FIGURE 1. Diagram illustrating anatomic relationship of the hepatic ligaments suspending the liver from the dorsum.

is divided into the suprahepatic space and the infrahepatic space, and on the left side there are three spaces: suprahepatic, anterior infrahepatic, and posterior infrahepatic.

Why is it important to designate the actual site of a subphrenic abscess? The importance lies not only in diagnosis but also in management. Signs, symptoms and complications are very different in suprahepatic and in infrahepatic infections, particularly in those occurring on the right side.

Clinical Features of Subphrenic Abscess

Regardless of the site of a subphrenic abscess, abdominal as well as thoracic signs are common. However, when all the findings are confined to the chest the infection is suprahepatic. When an abscess is in the right suprahepatic space, thoracic symptoms predominate. When the infection is situated below the liver, abdominal symptoms are more common than thoracic symptoms. Both right and left suprahepatic infections give rise to complications, but infrahepatic infections are

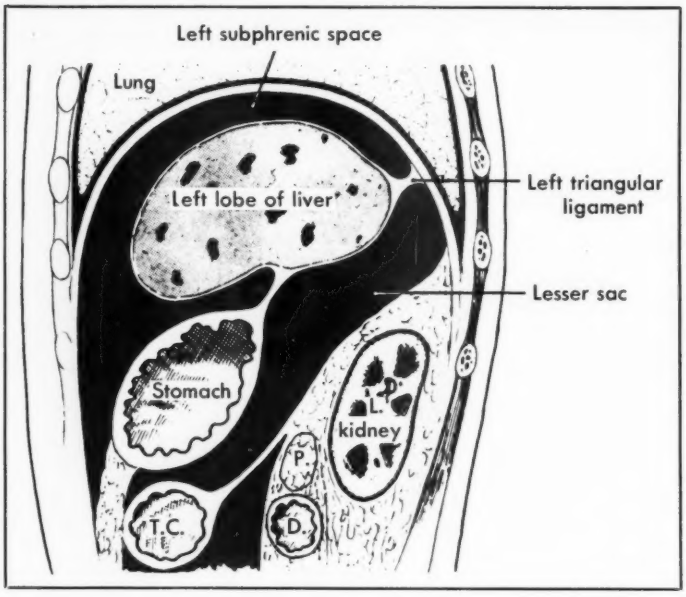

FIGURE 2. The suprahepatic and infrahepatic spaces on the left side. Note the two subhepatic spaces, the anterior one communicating widely with the suprahepatic space and the posterior one representing the lesser sac itself.

Figures 1 and 2 modified from Boyd, D. P.[1]

much less likely to do so, particularly on the right side.

In a typical left subphrenic abscess it is questionable whether we can truly distinguish between a suprahepatic and an anterior infrahepatic localization, because of the wide communication between these two spaces (figure 2) and also because in most instances the left lobe of the liver is quite small as it lies under the left dome of the diaphragm.

Left subphrenic abscesses are much more common than is generally realized, and their clinical features are of considerable interest. Carter[4] in 1939 reported that right subphrenic abscess was three to four times more common than left subphrenic abscess. Ochsner and DeBakey,[5] in describing 3,608 cases, found that the left side was involved in more than one-fourth of them. Neuhof and Schlossmann[6] reported finding 33 left subphrenic abscesses and 51 on the right side, despite the fact that in the literature slight attention is paid to left-sided infection.

Right suprahepatic abscesses are confined inferiorly by the massive right lobe of the liver, while infections on the left side are bound by the more mobile stomach, spleen and left lobe of the liver. For these anatomic reasons, elevation of the diaphragm occurs less often in left subphrenic abscesses, and thoracic changes are also less common. Radiologic diagnosis is much more difficult on the left side than on the right. On the left side a slight elevation of the diaphragm is more likely to be overlooked. A rise on the right side accentuates the normal difference in height between the two diaphragmatic domes, whereas a similar rise on the left side diminishes this difference. Further, gas in a left-sided subphrenic abscess is often mistaken for gas in the stomach or the splenic flexure of the colon. In addition, left-sided involvement is much more likely to be multilocular, making adequate drainage more difficult. Another difference is that subphrenic abscess on the left side occurs much more commonly as a consequence of malignant disease such as cancer of the stomach, pancreas or colon.[2,6]

In 1956 at the meeting of the American Surgical Association, Gerwig and Blades[7] of Georgetown University emphasized the camouflaging effect of antibiotics. Patients who appeared to be in relatively good condition as long as bacterial suppression was exerted by means of chemotherapy became desperately ill within hours after the antibiotics were

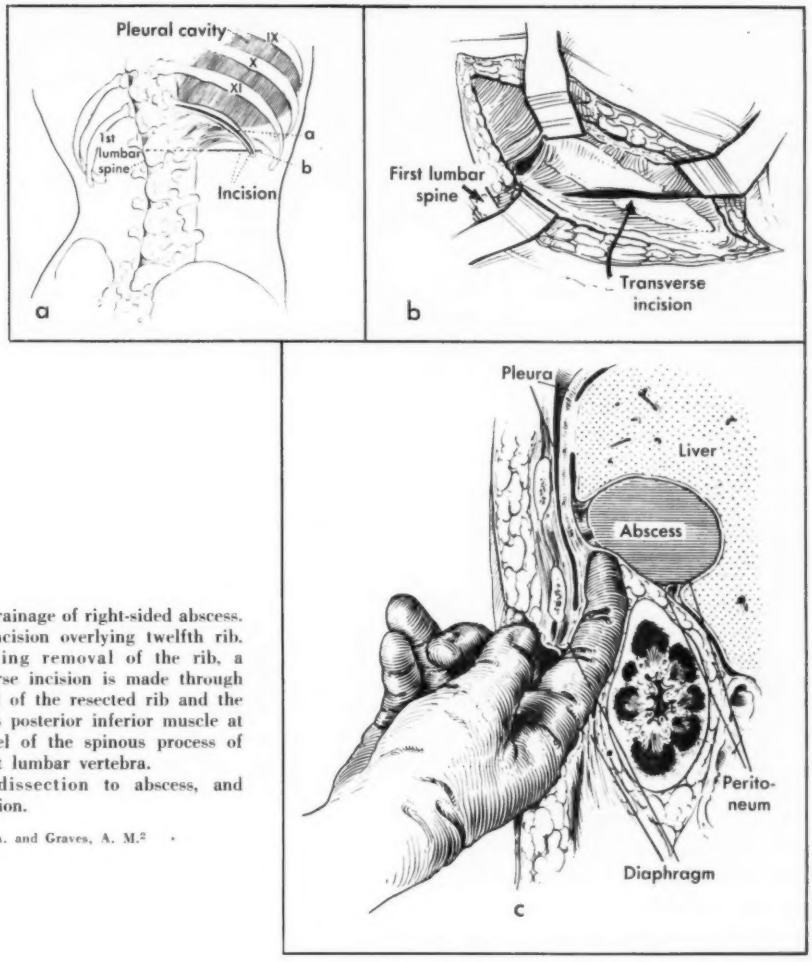

FIGURE 3. Steps in drainage of right-sided abscess.
a. Skin incision overlying twelfth rib.
b. Following removal of the rib, a transverse incision is made through the bed of the resected rib and the serratus posterior inferior muscle at the level of the spinous process of the first lumbar vertebra.
c. Blunt dissection to abscess, and evacuation.

Modified from Ochsner, A. and Graves, A. M.[2]

discontinued. In this regard, Altemeier has suggested discontinuing antibiotic therapy in these patients in order to allow for localization.

Etiologic Factors

Although some subphrenic infections gain access to the subdiaphragmatic area by way of the lymphatics and blood stream, the vast majority originate from extensions of intraperitoneal sepsis. Such extension is favored by the presence in the upper abdomen of a negative pressure fluctuating with respiration, as demonstrated by Overholt and Donchess[8] and by Drye.[9] Based on studies in man, it would appear that in the supine position the pressures in the lower abdomen and the upper abdomen are essentially equal, but in the sitting or the erect position the pressure in the lower abdominal cavity is as much as three times greater than that in the upper abdomen. An additional factor may be the ventral curvature of the lumbar spine in the supine position, resulting in a transverse ridge favoring the gravitation of pus distally into the pelvis and proximally toward the subdiaphragmatic region.

Subphrenic infection can originate from gallbladder disease or result from operations

in the region of the biliary tree or duodenum. Infections of the appendix, stomach and biliary region are most common sources of subphrenic abscesses. In most large series[2, 5, 10, 11] the appendix accounts for roughly one-third of the cases, the stomach and duodenum one-third, and the liver and bile passages 10 to 15 per cent.

Diagnosis

One should suspect the presence of subphrenic abscess in any patient with persistent unexplained fever associated with a history of recent intraperitoneal sepsis, a recent gastrointestinal operation or an intraperitoneal insult. Bear in mind also that the inciting factor may never be clearly established. In the early stages the condition is not always easy to diagnose. Not only may there be doubt as to whether the infection is above or below the diaphragm, but there may be a question also as to whether or not it will subside spontaneously without suppuration. Physical examination may be quite disappointing, with findings meager, inconstant or wanting. Occasionally, ileus or a sense of ill-being with slight fever is all that can be demonstrated.

The diagnosis of subphrenic abscess is made from one or more of the following points: (1) tenderness over the lower costal margin accentuated by compression of the rib margins; (2) elevation of the diaphragm on the affected side, together with manifestations of diaphragmatic irritation such as referred pain to the shoulder or neck, hiccup and discomfort with deep respiration; (3) roentgenologic confirmation of the clinical impression and degree of diaphragmatic excursion. The latter point, of course, includes fluoroscopic examination which may show elevation of the diaphragm or sluggish or paralyzed hemidiaphragm with a fluid level pocketed under the affected part.

Particularly in left-sided infection, it is occasionally helpful to give the patient a small amount of barium or water-soluble dye orally and carry out x-ray and fluoroscopic examinations with the patient in a slightly head-down or Trendelenburg position.[12] This may help to demonstrate an abnormal separation between the diaphragm and the gastric pouch suggestive of an abnormal collection. In addition, the presence of pleural effusion obscuring the costophrenic sinus is a helpful sign pointing to diaphragmatic inflammation, although this finding frequently is erroneously construed as a consequence of a pneumonic process. Plain and overexposed Bucky films in the anteroposterior and lateral projections also are quite useful.

One should remember that following laparotomy free air beneath the diaphragm can be demonstrated on x-rays for as long as 10 to 14 days, as Muller, Overholt and Pendergrass[13] have pointed out. Ochsner considers the presence of serous effusion over the diaphragm to be a late finding in neglected cases,[2] but other investigators[8, 14, 15] have not supported this contention.

Ochsner and DeBakey[5] believe that the two most helpful criteria are systemic manifestations of an unabating infection and persistence of localized tenderness in the subcostal region over the twelfth rib. They feel that these two findings justify exploration.

Aspiration of pus from the suspected area beneath the diaphragm as an adjunct to the diagnosis and treatment is mentioned only to condemn its use.[5, 10, 16-19]

Treatment

Once the diagnosis is established, the subphrenic abscess should be drained promptly. Even when the diagnosis is not clearly established, exploration often is justified on the basis that further delay may give rise to the complications of diaphragmatic perforation, empyema, pulmonary abscess, bronchial fistula, and rupture of the abscess leading to generalized peritonitis. Conservative management with intensive antibiotic therapy probably is permissible when the diagnosis is in doubt; however, if the tenderness and systemic manifestations of infection do not abate, exploration is justified.

Trendelenburg in 1883 advocated a transpleural approach to right-sided subdiaphragmatic abscess. This was attended by a high rate of mortality and was abandoned in favor of the two stage procedure in which the area

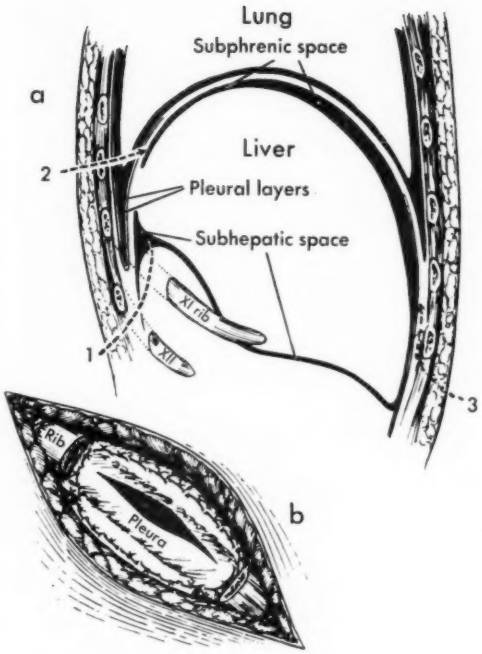

FIGURE 4. Methods of draining subphrenic abscesses.
1. Twelfth rib extraserous approach of Ochsner.
2. Trendelenburg's transpleural route. (Technic of suturing pleura to diaphragm is shown in insert "b.")
3. The anterior approach.

From Boyd, D. P.[1]

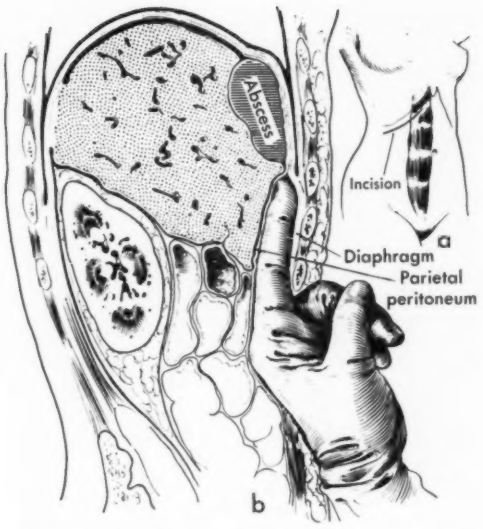

FIGURE 5. Extrapleural extraperitoneal approach to right anterior subphrenic abscess. Right anterior subhepatic abscess may be drained in the same manner or by the classic Ochsner approach.
a. Subcostal incision.
b. By blunt finger dissection the abscess cavity is reached without contamination of the general peritoneal cavity.

From Ochsner, A. and Graves, A. M.[2]

is packed and then subsequently (24 or 48 hours later) drainage is established. Ochsner[2] recommended the extraserous approach to the bed of the resected twelfth rib, and this procedure lowered the mortality rate significantly. In view of the anatomic relationships already mentioned, the common right posterior superior subphrenic infection actually may be a right posterior subhepatic one, and this latter type is easily drained by the Ochsner approach.

The classic method of drainage of a right-sided subphrenic abscess is illustrated in figure 3. An incision is made over the twelfth rib on the right side, and the rib is dissected and removed. After the fascia is divided, it is of utmost importance to take care to make the incision horizontal at the level of the first lumbar spinous process rather than obliquely down on the bed of the twelfth rib. Failure to observe this precaution will result in disastrous contamination of the pleural cavity. Melnikoff[20] demonstrated in cadavers that the pleura extends down on the right side below the twelfth rib in approximately 62 per cent, but it has never been shown to come down as low as the first lumbar spinous process. After making this transverse incision, by blunt dissection one approaches the abscess, enters it, and drains it with several Penrose drains or a hard rubber drain.

Boyd[1] has utilized the transpleural approach for the past 10 years and has treated more than 100 patients with subphrenic abscess in this manner. He feels there is no increase in complications associated with the transpleural approach. In this procedure the pleura is sutured down as shown in figure 4, circumferentially around the area where the incision

FIGURE 6. Case 1. Lateral roentgenogram of chest of 46 year old man 10 days after gastric resection for duodenal ulcer. Abnormal collection of air and fluid and elevated hemidiaphragm.

FIGURE 7. Case 2. Chest film of 58 year old woman five days after revision of anastomosis necessitated by recurrent lesion at anastomotic site following subtotal gastric resection for carcinoma of the stomach. Elevated right hemidiaphragm, pleural effusion, and abnormal loculation of fluid. Abscess subsequently developed on the left side.

will be made, and then the abscess is drained directly. Boyd feels that many abscesses, particularly those originating from pancreatitis or from operations involving the spleen, require drainage transpleurally. Advocates of the transpleural approach argue that it is superior because it affords more direct access to the involved area and minimizes contamination of the pleural cavity. They contend that such contamination rarely occurs, but this contention appears to be erroneous in view of the fact that the pleural cavity was contaminated in 32 per cent of cases so drained at the Massachusetts General Hospital and reported by Faxon.[10]

While other surgeons who advocate a delayed two stage procedure minimize the possibility of pneumothorax and pleural contamination, it appears to be less desirable to subject the patient who is debilitated to two separate operations, even though they are relatively minor. The retroperitoneal type of approach as depicted in figure 3 probably gives adequate dependent drainage of the abscess with the least amount of contamination.

A right anterior subphrenic abscess may be approached through a subcostal incision going extraperitoneally and extrapleurally (Ochsner), as shown in figure 5. A right anterior subhepatic abscess is also easily reached by this approach, which was first suggested by Clairmont and Meyer.[21]

In our clinic the method described as the four hole suction tip exploration is used by some surgeons. It was initiated by Dr. Owen H. Wangensteen. A short subcostal incision is made under local anesthesia. Following entry into the general peritoneal cavity, a long-handled four hole suction tip (Yankauer suction tube) is inserted and exploration is made over the dome of the liver and beneath the liver on the right side. If an abscess cavity is encountered, it is drained and Penrose drains are left in place and brought out through separate stab wounds. A similar procedure is carried out on the left side, and if no abscess

FIGURE 8. Case 3. X-ray of 53 year old man five months after partial colectomy for carcinoma of cecum. Subhepatic abscess was drained through an anterior approach. Recurrent tumor mass was excised radically, with excellent palliation.

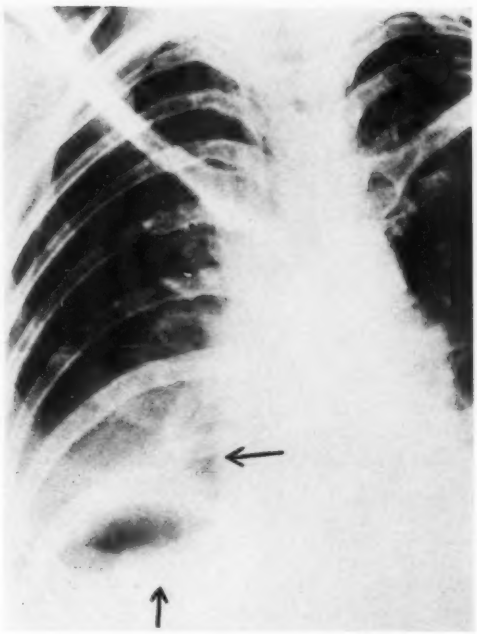

FIGURE 9. Case 4. Right subphrenic abscess in 84 year old woman three weeks after operation for biliary tract disease. Pneumonic changes, obliteration of costophrenic sinus, and elevation of right hemidiaphragm.

cavity is encountered, two smaller incisions are made lower in the abdomen under local anesthesia for similar exploration of the pelvis and the lateral gutters. This method is used at our hospital because of the high rate of mortality associated with undiagnosed subphrenic abscess; it is both a therapeutic and a diagnostic maneuver.

Mortality Rate

Obviously the mortality rate associated with subphrenic abscess depends on a number of factors such as the patient's age and condition, the antecedent course, the nature of the infecting organism, and the site and possible complication of the abscess itself. In general the mortality rate ranges from 20 to 30 per cent in various series. In one series the mortality rate associated with transperitoneal drainage was 55 per cent compared with 27 per cent for retroperitoneal drainage.[10] In Harley's[11] series the mortality rate ranged from 13 per cent for posterior drainage to 37 per cent for anterior drainage. Extraserous methods of drainage in another series were associated with a death rate of 11 per cent, and a threefold increase in mortality attended the transserous approach.

Illustrative Cases

Case 1—A 46 year old man underwent a Billroth II gastric resection because of duodenal ulcer. Ten days postoperatively his temperature rose to 104° F.; he had pain in the right shoulder and tenderness over the right costal margin, and a lateral roentgenogram (figure 6) showed an abnormal collection of air and fluid. The abscess was drained by the Ochsner method. Approximately 700 cc. of pus was removed. The patient recovered uneventfully.

Case 2—A 58 year old woman underwent subtotal gastric resection because of carcinoma of the stomach. A recurrent lesion developed at the anastomotic site, and the anastomosis was revised. Five days later the

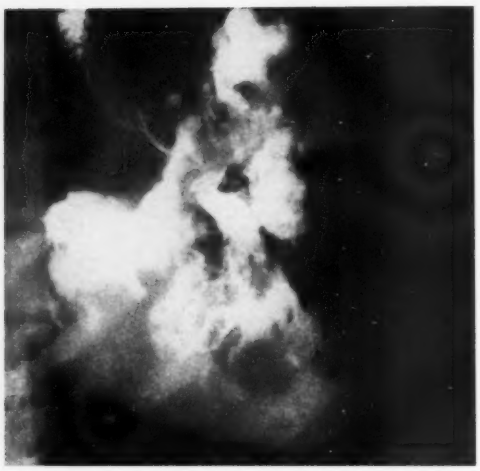

FIGURE 10. Case 5. Gastrografin study in 38 year old man who had undergone segmental gastrectomy seven days previously. Disruption of gastrointestinal continuity and well-established left subphrenic abscess. Adequate drainage plus nasogastric suction led to recovery.

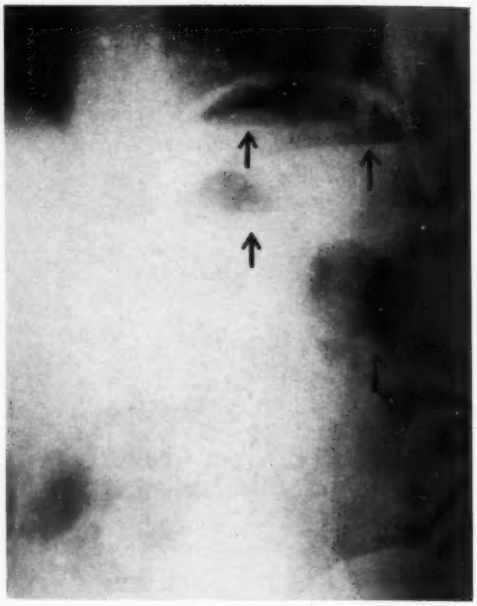

FIGURE 11. Case 6. Multiple loculated air-fluid level demonstrated by upright film of abdomen of 32 year old man five days after perforation of duodenal ulcer. Despite adequate drainage of left-sided lesion, patient died of Gram-negative septicemia four days after evacuation of abscess.

patient's temperature rose and the leukocyte count was 17,000. Elevation of the right dome of the diaphragm, pleural effusion and an abnormal loculation were noted in a roentgenogram (figure 7). By the Ochsner approach, 2000 cc. of pus was removed from the right side. Then an abscess developed on the left side and an additional 500 cc. of pus was removed. About 12 days later, another 300 cc. of pus was removed from the right side.

Case 3—A 53 year old man underwent partial colectomy for carcinoma of the cecum at another hospital. During the ensuing five months he noticed a progressively enlarging mass in the right side with involvement of the skin, and chills, fever and a vague sense of ill-being. When he arrived at our hospital his temperature was 106° F. and his leukocyte count was 25,000. His x-ray is reproduced in figure 8. Through an anterior approach, more than a liter of pus was drained from the subhepatic space, and subsequently Dr. Wangensteen resected the entire recurrent mass as well as a portion of the abdominal wall. Since dismissal from the hospital the patient has gained 28 lb.

Case 4—An 84 year old woman underwent cholecystectomy, exploration of the common duct, and duodenostomy for calculi. Three weeks after operation her temperature was elevated, leukocytosis was present, and elevation of the diaphragm and tenderness were noted (figure 9). By anterior drainage, 200 cc. of a purulent material was removed. Through the Ochsner approach, an additional 1000 cc. was removed. Three weeks later it was necessary to reopen the posterior area and remove another 500 cc.

Case 5—A 38 year old man had a perforated duodenal ulcer which was treated at another hospital. Subsequently a subphrenic abscess developed and he was referred to us. Drainage was carried out. Later, a retrocecal abscess formed and was drained. After a convalescent period the patient underwent gastrectomy. Postoperatively the patient did poorly, and seven days after gastrectomy his condition was critical. Roentgenograms taken

FIGURE 12. Case 7. Pneumonic changes associated with elevated right hemidiaphragm and abnormal collection of fluid and air in subphrenic region. The patient, a 13 year old girl, had a ruptured appendix which led to formation of an abscess.

after administration of GASTROGRAFIN®, a water-soluble dye, revealed gross discontinuity of the gastric anastomosis and a well-established left subphrenic abscess (figure 10). This was drained, and the patient made a good recovery.

Case 6—A 32 year old man was seen at our hospital five days after perforation of a duodenal ulcer. The leukocyte count was normal (6500) with 77 per cent neutrophils. A left-sided lesion with the loculated pattern seen in figure 11 was drained adequately. However, the patient died four days later from Gram-negative septicemia.

Case 7—This is a pathetic case which concerns a 13 year old girl. Her story can be reconstructed as follows. When first seen, she had had vague abdominal discomfort, fever, chills and some jaundice for about three weeks. She had a ruptured appendix which

FIGURE 13. Case 7. The subphrenic abscess was complicated by rupture of the diaphragm with formation of a pulmonary abscess and a bronchobiliary fistula. After multiple operative procedures, the patient is in reasonably good health.

led to formation of an abscess. Pyelophlebitis with thrombosis of the portal veins also developed and, secondarily, a hepatic abscess with a subphrenic abscess. Some of the pneumonic changes associated with subphrenic abscess can be seen in her x-ray (figure 12). The hepatic and subphrenic abscesses were drained, but the abscess had perforated the diaphragm and a pulmonary abscess as well as a bronchobiliary fistula had developed (figure 13). After drainage procedures were carried out for all the abscesses, esophageal varices secondary to portal hypertension developed. Because of the ensuing esophageal bleeding, splenectomy was performed and a splenorenal shunt accomplished. The portal pressure dropped from 47 to 27 cm. of water, but bleeding recurred. Partial esophagectomy, partial gastrectomy and esophagoantrostomy were performed, but intermittent bleeding continued. About a year ago she underwent esophageal resection with resection of the remaining antrum and a jejunal interposition operation. She has continued to do very well without subsequent bleeding, but one can see the tremendous amount of emotional as well as physical trauma this little girl has suffered, to say nothing of the cost of hospitalization.

The bill for blood alone during her periods of hospitalization was more than $2500. So the importance of early diagnosis and of prevention of subphrenic abscess is apparent.

Discussion

QUESTION: I wonder if you have had any experience with injury of the pancreas postoperatively. As the abscess tends to localize on the left, it may be difficult to diagnose, and if it is neglected or if it persists it may lead to death from infection and from thrombosis of the splenic vein and portal vein with pulmonary embolism.

I noticed in some of the illustrations that it is difficult sometimes to distinguish between air which may be in an abscess cavity and air which may be in a loop of bowel. From my experience this distinction does not seem to be so important from the point of view of the final diagnosis, because frequently in the presence of an abscess in this region a localized ileus seems to develop in a loop of intestine. So I think if you see a persistent loop of bowel on repeated films and cannot find a little air or feces which you think are in the abscess, this should be an important suggestion that the patient may well have an abscess.

DR. YONEHIRO: I think you have answered the second part of the question very adequately yourself. What you say is quite true. As far as ultimate management is concerned, the distinction is not very important. Usually there are ancillary findings of tenderness, ileus or fever.

In regard to your question about injury of the pancreas, more and more stress is being placed on this organ as a source of subphrenic abscess. It has also been stressed that acute pancreatitis, secondary to pancreatic resection, is seen more often today than it was previously; consequently, infection with abscess formation in the lesser sac is also increasing. Occasionally, if thin barium or Gastrografin is given and the abscess is large enough, a lateral view might demonstrate it. In general the tip-off to the presence of subphrenic abscess comes from an over-all assessment of the patient and an awareness of some of the features of this complication such as tenderness, failure to do well postoperatively, and a vague sense of ill-being. As Dr. Varco advocates,[12] in equivocal cases one is justified in performing an exploratory operation, because the risk of such exploration is much less than the risk of possible progression to phrenic rupture or other complications.

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Current Concepts in the Management of Intestinal Obstruction

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INTESTINAL obstruction continues to be one of the most common and most dangerous conditions of abdominal surgery. By prompt diagnosis and immediate proper therapy, the serious sequelae and disastrous outcome may be avoided. Although the term "intestinal obstruction" has come to be employed mainly to describe the mechanical type of obstruction, we should not lose sight of the fact that any interference with the passage of intestinal content along the lumen of the alimentary canal is an intestinal obstruction. In addition to the mechanical type, intestinal obstruction includes paralytic (inhibitory or adynamic) ileus as well as spastic (dynamic) ileus, which would be classed as obstructions that pertain to nervous imbalance. There is a third group, which is most difficult to manage, namely, vascular obstruction.

It is necessary to distinguish between obstructions of the small bowel and of the large bowel and to reserve the terms "high" and "low" for obstructions occurring at different levels of the small intestine. Most important in the diagnosis of intestinal obstruction is differentiation of strangulating and simple or nonstrangulating obstructions. Strangulation leads to gross gangrene of the affected intestinal segment, with subsequent perforation, peritonitis and death. However, nonstrangulating or simple obstruction, unless recognized early and managed promptly, eventually can reach an irreversible state leading to death. The surgeon constantly must keep in mind the risk of strangulation in every patient with mechanical intestinal obstruction. In nonstrangulating or simple obstruction it is possible for the circulation through the intestinal wall to become impaired, resulting in necrosis.

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The progressive distention associated with the increase in intraluminal tension may lead to this picture. However, usually this is a late effect in simple obstruction except in so-called closed-loop obstruction.

The use of such terms as "acute," "chronic," "complete" and "partial" may assist in describing the problem. An obstruction is termed "chronic" when it is partial and intermittent or recurrent. Since any obstructive episode is a menace to the patient, it is safer to consider all obstructions or threats of obstruction as acute. The term "chronic obstruction" frequently lulls the physician into a false sense of security because of its insidious onset; this is particularly true in certain types of colonic obstruction.

A most important fact to keep in mind is that the characteristics of an intestinal obstruction, such as signs and symptoms, often change as time passes after the onset. An obstruction may begin as a simple type and eventually progress to strangulation secondary to distention and other added mechanical factors. Treatment should be governed accordingly, and if operative measures are deferred on the basis that an obstruction is a simple type, the possibility that strangulation may have intervened should be reassessed at frequent intervals.

Mechanical Obstruction

Approximately two-thirds of all intestinal obstructions arise either from a strangulated hernia or from acquired or congenital adhesion bands. In adult men, strangulation of an inguinal hernia is most frequently the source, as opposed to strangulation of a femoral or umbilical hernia in women. As the middle and older age periods are approached, the incidence of obstruction caused by cancer increases greatly. Carcinoma accounts for only 10 per cent of all intestinal obstructions but is responsible for approximately 70 per cent of obstructions of the large bowel. Except for ileocolic intussusception in small children and the occasional cases of imperforate anus in newborn infants, obstruction of the large bowel is relatively rare in the younger age groups. Next in order of frequency to carcinoma as a cause of colonic obstruction is volvulus of the sigmoid colon, which accounts for perhaps one of every six acute obstructions of the large bowel.

In strangulating obstruction the immediate danger is readily apparent. If the strangulated loop is not removed, necrosis and dissolution will occur, resulting in overwhelming peritonitis. In simple and nonstrangulating obstruction the dangers are real but not apparent at first. These dangers stem from distention and losses of water and electrolytes. If strangulation ensues it will be a result of this triad of lethal effects of mechanical obstruction. The hyperperistalsis of the bowel proximal to the mechanical obstruction results in trauma to the intestinal wall and leads to edema. This edema contributes to the increase in the degree of the obstruction and may change a partial obstruction to a complete one. Secretion into the intestinal tract is actually increased and normal reabsorptive power is lacking in obstruction. This combination of increased secretion and defective absorption is typical of the overdistended intestine and may be an irritative phenomenon secondary to the intestinal hyperactivity. The degree of distention of proximal intestine depends on the completeness of the obstruction and on the time that has elapsed since its onset. Except in high obstruction, such as that located in the jejunum, the accumulation of gas and fluid in the distended coils of the small intestine is sufficient to create a serious problem which results in mechanical interference with such vital functions as respiration and venous return.

In unrelieved intestinal obstruction the progressive increase in intraluminal pressure interferes with the flow of blood through the wall of the bowel. Anoxia ensues, affecting the mucous membrane first. This is characterized by increasing edema, and eventually actual necrosis extends through the entire thickness of the wall. This necrosis from excessive intraluminal tension is best observed in the "closed-loop" obstruction, which type is more frequently seen in colonic obstructions in patients who have competent ileocecal valves. The formation of putrefactive gases and the continued entry of ileal contents into

the colon may combine to distend the loop until the intraluminal tension is dangerously high, and if a normal ileocecal valve is present the result is a closed-loop obstruction. Decompression by operative means is necessary in order to avoid pressure or vascular necrosis and perforation.

The problems encountered in simple and strangulating obstructions of the intestine include a sizable loss of plasma which escapes through the edematous intestinal wall and into the peritoneum, intensifying the dehydration and adding to the approaching depletion of fluid and electrolytes. In relatively infrequent instances of obstructions arising very high in the small intestine, the vomiting which is immediate and constant results in a loss of chloride and dehydration or hypochloremic alkalosis. In lower obstruction, vomiting usually is intermittent, and here the loss of sodium equals or exceeds that of chloride, resulting in a hyponatremic acidosis. In addition, the loss of potassium in plasma is great and must be compensated for by parenteral replacement therapy.

In strangulating obstruction, loss of blood into the lumen of the involved bowel and weepage of plasma into the bowel and peritoneal cavity are much greater than was previously recognized. Such patients would be aided best by the administration of whole blood or plasma or both.

The escape of bacterial toxins through the wall of gangrenous intestine contributes a most deadly threat in this disease.

One can conclude that so long as the wall of the intestine is intact the chief dangers in obstruction of the lumen lie in the losses of water and electrolytes and the mounting intestinal distention. In contrast, in strangulating obstruction the sequelae to impairment constitute an immediate danger.

Diagnosis of Mechanical Intestinal Obstruction

The diagnosis of acute mechanical intestinal obstruction is based on the symptom triad of crampy abdominal pain, vomiting, and failure to pass gas or feces by rectum. A most constant observation on physical examination is an increase in peristaltic sounds. In early obstruction there may be only slight distention, occasional hyperperistalsis and moderate tympany on percussion. Significant leukocytosis usually is absent, and water or electrolyte losses usually are not sufficient to be reflected in chemical determinations. The most important laboratory test at this time is the roentgenographic examination of the abdomen.

The advent of strangulation in an obstruction of the small bowel produces sudden and dramatic changes which are easily recognized. At this point the surgical emergency is obvious. Flat and upright films of the abdomen are most helpful in determining the presence of obstruction and its level. The finding of free air under the diaphragm would suggest a perforation. The x-ray appearance sometimes may be typical for immediate identification of the mechanism causing the obstruction; this is particularly true in diagnosis of volvulus of the sigmoid.

Other peculiar configurations aid in the roentgenologic diagnosis of intussusception and malrotation. In some instances the concomitant use of barium as a contrast medium is helpful if the material is given as an enema, provided due care is exercised lest perforation occur. This technic should rarely be necessary, however.

The oral administration of barium to patients with intestinal obstruction is to be condemned. It has led to many deaths of patients having colonic obstructions, through operative and postoperative complications for which the barium was responsible. Information to be gained by the oral administration of barium is seldom worth the risks in these cases; when one weighs the advantages against the several risks, the procedure has little if any usefulness. Use of a thin barium mixture occasionally may be permissible in suspected pyloric or duodenal obstruction provided the barium can be recovered by lavage. The approximate site or level of obstruction often can be determined on the basis of the history and symptoms. In addition, scout films of the abdomen for localization of the obstruction permit a more intelligent surgical approach.

Management of Mechanical Intestinal Obstruction

During the past 25 years there has been a remarkable reduction in the over-all mortality rate in acute intestinal obstruction. A decrease from the former rate of more than 40 per cent to the present rate of about 10 per cent is a magnificent achievement. However, the fact that approximately 10 per cent of patients with intestinal obstruction still will die as a result of the disease is evidence of the critical dangers.

The discovery of antibiotics, development of improved surgical technics, and refinements in anesthesia have assisted in this reduction of mortality, but the chief responsible factors have been (1) decompression devices to prevent and correct intestinal distention and (2) more effective replacement therapy made possible by constantly increasing knowledge of fluid and electrolyte balance.

In the vast majority of patients the obstructing mechanism can be released only by operation, and therefore the treatment of intestinal obstruction remains primarily surgical. However, intestinal decompression and parenteral replacement therapy are vital supportive measures, often essential to both preoperative preparation and postoperative care.

Decompression of the small intestine as introduced by Dr. Wangensteen in 1931 at the University of Minnesota is still basically best performed by passing a tube through the nose or mouth into the stomach or upper intestine. Whether one wishes to use the nine hole Wangensteen or Levin tube or the variations of long intestinal tubes such as the Miller-Abbott and Smith tubes is of little consequence. One should not forget that it is much easier to prevent distention than to relieve it once it is established. Therefore, in all patients with suspected intestinal obstruction the immediate therapy should be the institution of continuous gastric aspiration.

The misuse and overuse of intestinal decompression deserve emphasis. Intestinal decompression should be employed as an adjunct in the treatment, not as the basic therapy itself. The delay incident to unsuccessful attempts to intubate the intestine may be very dangerous. Although laparotomy admittedly is hazardous in the presence of marked distention, that danger to the patient is not half as great as the danger arising from delay when strangulation is present or imminent. Intestinal decompression is primarily a method for combating distention, and its use has been libeled by the fact that in many instances constant attempts to substitute decompression for surgical operation as definitive treatment of obstruction have been reported. It is true that in a number of patients having early or incipient obstruction, such as certain types of obstruction of the small intestine, decompression actually does serve to release the obstructing mechanism, thus avoiding the need for an emergency surgical procedure. Because of this, the tube has been overused, and decompression by this means has frequently been called by some writers "nonoperative management of bowel obstruction."

It is almost impossible to select patients in whom it is safe to defer operation while a satisfactory period of decompression therapy is attempted. Lack of appreciation of this difficulty has continued to lead to costly misuses of decompression as a tentative substitute for surgery. The cessation of pain and vomiting which follows the institution of decompression and the temporary improvement of the patient's condition brought about by administration of water and electrolytes may give a false sense of security and be interpreted as an indication of relief of obstruction. Actually this is only relief of certain symptoms. In many cases operation is postponed unduly until subsequent deterioration of the patient's condition finally forces an operation on the surgeon at a time when the hazards are greater than they would have been earlier. Exploratory laparotomy in such cases may reveal unrecognized strangulation which would have been prevented by early use of the surgical scalpel.

Decompression of the large intestine can be accomplished only by surgical means, that is, performance of transverse colostomy or cecostomy, depending on the location of the obstruction. Any attempt to decompress the

colon by the use of long intestinal tubes should be condemned. Use of nasogastric suction, however, is effective as an adjunct, since by recovering swallowed air it prevents additional distention of the proximal small intestine and the colon.

Prevention of water and electrolyte imbalance and correction of existing deficits are a main concern in the treatment of every patient with intestinal obstruction. The level of the obstruction influences replacement requirements. In high obstructions, losses by vomiting usually are copious, while in colonic obstructions there may be no vomiting. The interval since the onset of obstruction is another important consideration. Replacement needs in the early stages are correspondingly less than at later stages. The possible presence of strangulation limits the period of delay available to effect adequate replacement.

The management of obstruction of the small intestine necessitates the correction of dehydration which results from lack of oral intake associated with loss of intestinal secretions. Examination of the urine for color, volume and specific gravity may provide a rough measure of the extent of the dehydration. This can be corrected by intravenous administration of adequate water and sodium chloride. Glucose is added to reduce the caloric deficit. The appearance of a dilute urine which contains chloride ordinarily indicates that water balance has been restored. Determination of the carbon dioxide combining power of the blood will reveal the extent of acidosis or alkalosis. Potassium replacement is deferred until the output of urine is good, and in emergencies it often can be postponed until the postoperative period. Vitamins A, B, C and D are added to the intravenous infusions. The need for adequate blood transfusions in the preoperative preparation of many patients having obstructions of the small intestine has been most apparent in recent years. Loss of whole blood into the lumen of strangulated intestine or loss of plasma into the wall of the edematous bowel necessitates replacement. The transfusion of blood or plasma assists in preparing patients for operation when strangulation is suspected or obvious.

Obstructions of the large bowel usually present problems in regard to correction of physiologic deficits which are different from those in obstructions of the small bowel. Vomiting is not a prominent feature, and therefore losses of water and electrolytes usually are not acute. However, since obstruction of the large bowel is more common in older persons, who frequently have a chronic illness, the chief concern is with replacement of blood, proteins and vitamins rather than with administration of water and electrolytes.

If complete obstruction of the colon has not ensued at the time the surgeon sees the patient, it is advisable to correct malnutrition and anemia adequately before operation. This period may also permit preparation of the colon with antibiotics. If acute obstruction of the colon is present, however, time should not be wasted with complete fluid and electrolyte replacement or antibiotic protection. Rather, the chief concern is assuring adequate decompression. Time should be saved by performing a simple type of decompression operation on the colon, such as transverse colostomy. Fortunately, many patients have obstructions of the large bowel of such nature, permitting the postponement of definitive treatment to a later date.

Rectal examination is essential in all cases of suspected intestinal obstruction. Impactions and rectal and pelvic tumors, if discovered, frequently alter the entire plan of treatment. A great many patients having obstruction will have been given one or more enemas in the process of establishment of a diagnosis. Continued passage of gas and liquid following such enemas may give the erroneous impression that the obstruction is incomplete. The enemas may be cleansing that part of the bowel distal to the obstruction, which contained feces and gas before obstruction occurred. The use of an enema is not devoid of danger, because of possible perforation.

Antibiotics may be helpful in the treatment of strangulating obstructions in that they may delay the onset of necrosis as well as combat its ill effects. For parenteral administration, a combination of penicillin and streptomycin along with one of the wide-spectrum anti-

biotics such as ACHROMYCIN® or CHLOROMYCETIN® is of value.

In cases of complete obstruction one must first determine whether strangulation is or is not present. If strangulation is considered to be present or imminent, operative management without undue delay is mandatory. During the hour that it may take to prepare the operating room and induce anesthesia, one may administer saline, blood, antibiotics and plasma. This supportive therapy is continued during and after operation. In the presence of recognized strangulation, however, any greater delay is not justified and the correction of water and electrolyte depletion can continue during and after operation. Liberal use of blood transfusions in such patients helps to sustain them during the emergency.

Emergency surgical management is also required when acute colonic obstruction is associated with marked distention. Delay is apt to result in necrosis and perforation, especially if the obstruction is of the closed-loop type due to a competent ileocecal valve.

If the surgeon considers the obstruction to be simple and nonstrangulating, he must remain alert to the possibility that it may change in character. He should reassess the patient frequently for the possible presence of strangulation or progression of the obstruction. However, it is often difficult to recognize the advent of strangulation, and it is wise to avoid procrastination by setting a time limit for the preparation of the patient, to be followed by surgical intervention. This is particularly important in cases of patients being given a trial of decompression therapy. A relenting of the distention may mask some of the many symptoms of obstruction. Some surgeons have advised immediate operation if the obstruction is not relieved within a six hour period, since that length of time ordinarily will suffice for adequate parenteral replacement.

Patients with early simple intestinal obstruction do not require too much in the way of replacement therapy. Since the distention is not yet severe, they are ideal candidates for immediate operative relief, and with present-day conditions the surgical risk is not too great. We feel that this is a good basis for recommending prompt operation for all patients with early obstruction. We realize that this will mean that a few patients will be operated on unnecessarily, but the risk will be slight compared with the dangers of delay.

Early postoperative obstructions should be considered separately, since it may be impossible to observe the time limitations recommended for obstructions in general. After major abdominal surgical procedures, reflex inhibition of intestinal motility occurs for 24 to 72 hours, following which patients have symptoms suggesting mechanical obstruction due to return of intestinal tonicity. However, inflammation and edema play important roles in the early postoperative period, and a number of postoperative obstructions may be mechanical in a relative nature and can be relieved immediately by decompression therapy. This fact plus a widely held impression that there is little risk of strangulation have resulted in overconfidence in dealing with such cases. Actually, strangulation does occur in 10 per cent or more of patients with early postoperative obstruction. Thus, once obstruction is diagnosed in these cases, surgical exploration should be prompt if intubation fails to relieve it.

The operative treatment of mechanical obstruction requires the restoration of physiologic continuity of the bowel, and the surgeon should also be concerned with preventing recurrences of obstruction. Marked distention always makes surgery technically difficult, resulting in greater trauma and hazard to the patient. When operation is performed in the presence of severe distention, the distended intestinal loops may be deflated by direct suction aspiration, employing the closed aseptic technic as described by Wangensteen in which various trocars of different design are introduced through the bowel wall. We have adopted the use of the Smith tube passed through the mouth and then (with the abdomen opened) guided by the surgeon's hands through the stomach and pylorus into the small bowel down to approximately 4 or 5 in. from the obstructing site in the small bowel. If an anastomosis of small bowel to small bowel or of small bowel to colon has been

performed, it is wise to have the Smith tube just proximal to this anastomotic site for decompression, thus preventing compromising the blood supply due to distention.

Strangulation requires surgical excision. If strangulation occurs in the small intestine, a primary excision and anastomosis in one operative procedure are preferred. In strangulated colonic obstructions such as volvulus of the sigmoid, however, experience has demonstrated that it is best to exteriorize or resect and exteriorize these loops with the intention of performing anastomosis at a later date. In addition, patients with carcinoma or diverticulitis, who often are debilitated, are usually better treated by primary decompression of the distended colon by the performance of colostomy, with excision and primary anastomosis later. The emergency situation having been relieved, time is afforded for adequate restoration of the patient by replacement therapy and for preparation of the intestine with antibiotics. Definitive treatment of the causative lesion can be performed later.

Neurogenic Obstruction (Intestinal Obstruction Due to Nervous Imbalance)

Paralytic (inhibitory) ileus is a term commonly used in referring to impairment of intestinal peristalsis due to an inflammatory reaction. It is most often seen in peritonitis. The intestinal activity appears to be inhibited by an overactive sympathetic nervous system. However, this condition may accompany traumatic or infectious lesions which are extraperitoneal or even extraabdominal. Such conditions as strangulation of the intestine, renal colic, gallbladder colic, torsion of an ovarian cyst, and strangulation of the spermatic cord may be etiologic agents. Ileus may be coincident with a generalized toxic state such as uremia or may be seen in severe electrolytic imbalance, especially hypochloremia. Injuries causing fractures about the ribs or spine or retroperitoneal hemorrhage due to irritation of spinal nerves and nerve roots may commonly produce abdominal pain, muscular spasm, vomiting and ileus. The temporary state of inhibitory ileus after abdominal surgical procedures, a result of exposure of the peritoneal surfaces and manipulation of the bowel, is well known.

The clinical picture is one of extreme meteorism, absence of colicky pain, a distended and silent abdomen, and generalized mild abdominal tenderness due to distention. Abdominal x-rays showing distended loops of small and large bowel plus the absence of bowel sounds on auscultation are pathognomonic of this disease.

The management of paralytic ileus is its prevention. This is best effected by intestinal decompression employing a gastric tube during the early postoperative period. It is much easier to prevent distention than to relieve it.

The severe form of paralytic ileus is that accompanying bacterial or chemical peritonitis. This is best treated by the use of gastrointestinal intubation, antibiotics, blood and plasma, and treatment of the primary disease. This form of paralytic ileus frequently is a result of perforation of a viscus such as the colon, stomach, gallbladder or appendix or intraabdominal abscesses.

Routine use of gastric suction after major abdominal surgical procedures frequently will prevent the unnecessary occurrence of ileus and will minimize its extent if it should occur. Operation offers little in such cases. The use of PROSTIGMINE® usually is of little value.

Spastic or dynamic ileus may be confused with mechanical obstruction. This form of ileus is due to spastic contraction of a segment of intestine, in contrast to the relaxation noted in inhibitory ileus. It is usually functional in nature (neurasthenia and hysteria), and a test with atropine or other antispasmodics may aid in differentiation. Most cases involve the colon. Other causes include lead colic, trauma, gallstone ileus, foreign bodies, worms, ulcers, renal colic and infectious fevers.

Vascular Obstruction (Intestinal Obstruction Due to Mesenteric Thrombosis and Embolism)

"Vascular obstruction" applies to the relatively infrequent obstruction caused by mesenteric vascular occlusion, either arterial or venous. Most commonly the superior mesenteric artery is involved. Embolism of the su-

3. Abuse of morphine (analgesics). Morphine abolishes intestinal colic, the pathognomonic sign of intestinal obstruction. It also increases peristalsis, resulting in increased borborygmi. Therefore, it is difficult to evaluate the signs, and it is best to employ the surgical scalpel rather than the hypodermic syringe.

4. Deception of apparently effectual catharsis in partial obstruction. The expulsion of a stool after administration of a cathartic does not mean the bowel is unobstructed. Continuation of the pain indicates that the obstruction is still present. Use of cathartics, like morphine, is not to be recommended and may be dangerous.

5. Overuse of decompression. Decompression should not be used as a substitute for surgery. The delay incident to unsuccessful attempts to intubate the intestine may be very dangerous.

Discussion

QUESTION: Do you ever have any trouble removing the Miller-Abbott tube?

DR. SHAHON: I have heard of knots being tied in the bowel following attempts to remove the Miller-Abbott tube. We tend to use the Smith tube rather than the Miller-Abbott tube, so our experience is limited. However, I have never noted any difficulty in removing a Miller-Abbott tube.

QUESTION: Do you ever use any medical therapy to promote peristalsis?

DR. SHAHON: Yes, Prostigmine or similar drugs. But I have not been particularly impressed with them. I do not see how one can make a bowel work when it is inhibitory. I think the best treatment is the prevention of gaseous distention postoperatively by the judicious use of the Levin tube and Wangensteen suction.

BOOKS RECEIVED

Books received are acknowledged, and, as space permits, those of principal interest to our readers are reviewed more extensively. Reviews appear in this issue starting on page A-146; additional listings are on pages 308, 313 and A-154.

The Medical Annual (1960). A yearbook of treatment and practitioners' index. Edited by R. Bodley Scott, F.R.C.P. and R. Milnes Walker, F.R.C.S., with 44 contributors. 572 pages, illustrated. 1960, John Wright & Sons Ltd., Bristol. Distributed by The Williams & Wilkins Company, Baltimore. $9.00.

Stuttering; and What You Can Do About It. By Wendell Johnson, Professor of Speech Pathology and Psychology, State University of Iowa, Iowa City. 208 pages. 1961, University of Minnesota Press, Minneapolis. $3.95.

Dermatology; Diagnosis and Treatment. By Marion B. Sulzberger, M.D., Professor and Chairman, Department of Dermatology and Syphilology, New York University School of Medicine and New York University Post-Graduate Medical School, Jack Wolf, M.D., Attending Dermatologist, Grand Central Hospital, and Victor H. Witten, M.D., Associate Clinical Professor of Dermatology and Syphilology, New York University Post-Graduate Medical School, with the collaboration of Alfred W. Kopf, M.D., Assistant Clinical Professor of Dermatology and Syphilology, New York University Post-Graduate Medical School, New York. Ed. 2. 615 pages, illustrated. 1961, The Year Book Publishers, Inc., Chicago. $14.00.

Valvular Disease of the Heart in Old Age. By P. D. Bedford, M.D., Consultant Physician, and F. I. Caird, D.M., Medical Registrar, Cowley Road Hospital, Oxford, England. 194 pages with 38 illustrations. 1960, Little, Brown & Company, Boston. $7.50.

Surgical Diseases of the Pancreas. By John M. Howard, M.D., Professor and Chairman, Department of Surgery, Hahnemann Medical College and Hospital, Philadelphia, and George L. Jordan, Jr., M.D., Associate Professor of Surgery, Baylor University College of Medicine, Houston, with nine contributors. 607 pages with 197 illustrations. 1960, J. B. Lippincott Company, Philadelphia and Montreal. $20.00.

Cutaneous Manifestations of the Reticuloendothelial Granulomas. American Lecture Series. Edited by Samuel M. Bluefarb, M.D., Associate Professor of Dermatology, Northwestern University Medical School, Chicago, with eight contributors. 442 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $14.50.

Variations on a Theme by Sydenham; Smallpox. By P. B. Wilkinson, M.R.C.P. 75 pages with 69 illustrations. 1959, John Wright and Sons Ltd., Bristol. Distributed by The Williams & Wilkins Company, Baltimore. $4.25.

The Surgical Treatment of Portal Hypertension, Bleeding Esophageal Varices and Ascites. American Lecture Series. By M. Judson Mackby, M.D., Staff Surgeon, Kaiser Foundation Hospital, San Francisco. 250 pages with 49 illustrations. 1960, Charles C Thomas, Springfield, Illinois. $10.50.

perior mesenteric artery may occur in patients having mural thrombi, vegetations on the heart valves, acute myocardial infarct, or auricular fibrillation. Chronic thrombosis of the artery is rare. Mesenteric venous occlusion commonly occurs as a thrombophlebitis secondary to abdominal abscess (pylephlebitis). This may result from abdominal trauma or from portal venous stasis such as occurs in polycythemia.

Vascular obstruction is probably the most difficult entity to diagnose. The only feature that is typical about vascular obstruction is its atypicalness. It may be insidious with surprisingly few symptoms or sudden in onset and catastrophic. In many cases there is a mild course with more than a week elapsing before the existence of a serious lesion is suspected.

The usual manifestations are severe abdominal pain, vomiting and diarrhea of sudden onset. The stools and vomitus occasionally contain blood, which usually indicates strangulated obstruction. Shock may be present. Progressive abdominal distention and absence of peristalsis are common. Frequently, abdominal tenderness and leukocytosis are present in the later stages.

X-rays of the abdomen may present almost any picture ranging from a normal interpretation to numerous gas-filled and fluid-filled loops of small and large intestine. The finding of a gasless abdomen on an abdominal x-ray should make one suspect vascular obstruction. Frequently the presence of large quantities of fluid in the peritoneal cavity may be noted on the x-ray.

Mesenteric occlusion seldom is diagnosed prior to operation unless one has reason to suspect embolism or venous thrombosis from the patient's history. The prognosis usually is poor, and treatment is best provided by immediate resection of the gangrenous intestine and re-establishment of bowel continuity by anastomosis. When the superior mesenteric vessels are involved, the resection includes the segment from the duodenal-jejunal flexure to the midtransverse colon. These patients are nutritional cripples and survive by utilization of their body fat.

Summary

In the diagnosis of intestinal obstruction the physician should ask himself the following questions:

1. Is obstruction present? (Common symptoms: pain, crampy and colicky; vomiting, frequent and copious; distention. Signs: early, none; late, obvious.)

2. Where is the obstruction? (X-ray is the best means of localization.)

3. Is the obstruction complete or incomplete? (If there is no gas in the colon, obstruction is complete.)

4. What is the manner of the obstruction (simple or strangulating)? (Auscultation and palpation; leukocytosis.)

Intestinal colic without abdominal tenderness signifies presence of a simple obstruction. Intestinal colic with accompanying abdominal tenderness suggests a strangulating obstruction. *Abdominal tenderness is the most reliable sign distinguishing between simple and strangulating obstructions.* However, abdominal tenderness can be present in a case of simple obstruction, and it is wise, therefore, to regard all obstructions exhibiting definite evidence of abdominal tenderness as instances of potential strangulation.

Factors causing delay in diagnosis are:

1. Absence of local physical findings. Simple obstruction frequently does not give rise to local physical findings. Thus the impression is that a trivial condition is present. Simple intestinal obstruction is the only serious acute lesion that does not give rise to abdominal tenderness. When there is a lack of local physical findings in a patient with abdominal pain, nausea and vomiting, one should suspect the presence of intestinal obstruction.

2. Mistrust in enemas. It has often been said that total obstipation characterizes intestinal obstruction. Only in complete low obstruction is total obstipation certain. The bowel distal to the obstruction is physiologically and anatomically normal. In incomplete obstruction, gas may be passed per rectum. The passage of gas and feces after the administration of an enema does not rule out the presence of an obstruction.

commonly has a history of imbibing heavily of alcohol.

The acute esophageal perforation ordinarily penetrates into the left side of the chest. The patient usually will have some degree of mediastinal emphysema which can be seen quite clearly on a chest film. Management of this catastrophe requires (1) immediate treatment of the shock, (2) thoracotomy in the left side of the chest, (3) suture of the rent in the esophagus, (4) placement of a nasogastric tube past the site of the perforation into the stomach for decompression, and (5) the use of catheters attached to suction for expansion of the left lung and positive drainage of the pleural cavity. If the patient is seen early and if proper surgical and supportive therapy is given, he will get along well.

Duodenum—We have had substantial experience with perforation of duodenal ulcers. In 1957 we had 15 patients with perforated duodenal ulcer, in 1958 we had 11, and in 1959 we had 12. It is important in considering this catastrophe to keep in mind a few of the more likely conditions that can be confusing in the differential diagnosis. Pancreatitis is an example; we see a significant number of these cases too, and ordinarily we can be fairly sure our differentiation of the two acute problems is correct. Some of the helpful things in this regard will be mentioned by Dr. Strobel when he describes the roentgenographic findings. We have found that the serum amylase determination is very useful; and another test that can be helpful is a peritoneal tap, performed as advocated by Dr. Robert Zollinger. A small amount of saline is instilled in the peritoneal cavity and then reaspirated; the aspirated material is tested for amylase activity.

Ordinarily the onset of a duodenal perforation is so acute and characteristic that little more need be said about it here. Perhaps we should point out, however, that the region of maximal pain can be the right lower quadrant since spillage from the duodenum may run down the right gutter of the abdomen. With the history of sudden onset of pain in the epigastrium and the appearance of muscle guarding predominantly in the upper abdomen, we usually can orient our diagnosis to the correct site of the trouble.

Gallbladder—Compared with perforated duodenal ulcer, we have seen few cases of perforated gallbladder. One reason might be that we have long favored operation for cholecystitis during the acute phase of the disease. In those patients in whom exploration is carried out and a bile peritonitis is found secondary to rupture of the gallbladder, we recommend placement of a cholecystostomy tube and deferment of excision of the gallbladder until a later operation.

Renal calculi—Renal colic sometimes can present confusing findings. During the past year we have had three patients with renal colic due to renal calculi, and in each instance we were able to establish the correct diagnosis. One of the main points in differential diagnosis of this problem is the ultimate referral of the pain to the genitalia and the perineal area. Presence of red blood cells in the urine can be most helpful in clinching the diagnosis.

Thrombosis—Mesenteric thrombosis is a difficult diagnostic problem. It is acute and sudden in onset, and often the diagnosis can be established only by surgical exploration. There are times when we need to operate mainly on the basis of a high index of suspicion of bowel infarction in order to find a situation amenable to surgical correction.

Appendix—Perforated appendix will be discussed subsequently. In our hospital, at least, it is not usually too confusing in terms of differentiation from perforated duodenal ulcer and from other acute intraabdominal problems.

Chest problems—Occasionally, pneumonitis or pleurisy of severe degree can simulate an epigastric disorder and be mistaken for a perforation in the upper gastrointestinal tract. The routine chest film obtained at the time of admission of all patients aids materially in confirming our clinical impressions of chest problems after auscultation.

Now, I am going to ask Dr. Strobel to present briefly the case reports of three patients seen at Minneapolis General Hospital to illustrate diagnosis and management.

Acute Perforations of the Gastrointestinal Tract

CLAUDE R. HITCHCOCK* AND CLAIRE J. STROBEL†

University of Minnesota Medical School and Minneapolis General Hospital, Minneapolis

DR. CLAUDE R. HITCHCOCK: Wishing to "vitalize" this topic, which has become somewhat overworked lately, I have invited Dr. Claire Strobel, one of my senior residents on the surgical service at Minneapolis General Hospital, to help me with this presentation. Another reason for doing this is because I want to give you a true picture of our experience, and having one of my chief residents with me helps to keep me an entirely honest man.

To cover the topic of acute gastrointestinal perforations thoroughly, including etiology, differential diagnosis, management, pitfalls, and so on, for each area of the gastrointestinal tract, could well occupy an entire day. In the short time allotted, we are going to start with the esophagus and very quickly move down the gastrointestinal tract to try and give you a few pointers or helpful suggestions.

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CLAUDE R. HITCHCOCK

CLAIRE J. STROBEL

Esophagus—If your experience is like ours at Minneapolis General Hospital, you see few acute perforations of the esophagus. Each year more than 40,000 persons are hospitalized or seen as outpatients at Minneapolis General Hospital, and in the past several years we have seen only a few acute perforations of the esophagus. In other words it is very rare. It is more common, however, in men than in women. Usually it is the lower third of the esophagus that perforates acutely, and frequently the perforation occurs after an episode of retching and vomiting. The patient

FIGURE 1. Routine chest x-ray demonstrating free air under both sides of the diaphragm secondary to perforation of a duodenal ulcer.

Case 1: Duodenal Perforation

DR. CLAIRE J. STROBEL: A 43 year old man came to the hospital in October 1959 because of acute epigastric pain of eight hours' duration. He had experienced three episodes of vomiting and intermittent periods of mid-epigastric pain for about two days. He had some intolerance for fatty foods and occasionally had heartburn. His intake of alcohol was heavy, and he had been drinking the day before his illness began. An ulcer had not been diagnosed previously.

Blood pressure was normal, and the pulse rate was 88. The patient was perspiring freely. Physical findings were limited to the abdomen. It was rigid, and we noted rebound to the epigastrium and only a few hypoactive bowel sounds. The hemoglobin level was 13.7 gm. per cent, and the hematocrit reading was 41 per cent.

A chest x-ray showed what we thought was free air, but we were not quite sure. The x-ray in figure 1 is of another patient, and is presented to demonstrate this finding clearly. We have had several patients on whom we have operated after a diagnosis of perforated ulcer was made and in whom we were unable to see any free air in the chest film or upright abdominal film. In some of these instances I believe the perforation was too recent, or the patient did not sit up or stand up long enough for the air to gravitate upward under the diaphragm. A helpful adjunct for the diagnostician here is to obtain a film in the left lateral decubitus position; sometimes a small amount of free air can be seen between the liver and the abdominal wall—although one needs to be a little careful in this respect because the patient may have a fat pad that can be mistaken for free air.

The patient was taken to the operating room shortly after he was admitted. The abdomen was opened carefully with fluid in the incision to rule out free air, and no bubbles appeared. However, about 300 to 400 cc. of bile-stained material was aspirated from the abdominal cavity, and a perforation was noted in the anterior wall of the duodenum just distal to the pylorus. There was an exudate over the liver and stomach, and some loose adhesions were found between the stomach and the liver. We closed the duodenal perforation by plicating a tag of omentum over the opening and did nothing further with the ulcer. The abdomen was irrigated with about 5000 cc. of sterile saline and the incision was closed. Antibiotics were not given postoperatively, and the wound healed without infection in about seven days.

A culture of the material taken from the abdominal cavity grew alpha streptococci and *Staphylococcus albus*. About a week after operation, a test of gastric acidity performed on a grab specimen showed 68 degrees of free acid, 6 degrees of combined acid, and 74 degrees of total acidity. Three weeks later a subtotal (70 per cent) gastrectomy was performed, using the Billroth II procedure. The patient was dismissed from the hospital eight days later, and has had no further difficulty.

DR. HITCHCOCK: This case brings up several points. We believe that the first consideration in management of these problems is to suspect what you are dealing with. We place a nasal tube down immediately and apply suction, and then prompt steps are taken to correct the

hypovolemia and hemoconcentration which often are present if any number of hours have elapsed since the perforation. In our experience, these patients do not vomit very much and do not present the severe electrolytic disturbance of alkalosis on the basis of hypokaliemia and hypochloremia. Fairly severe hypovolemia, however, may be present due to massive accumulations of serous fluid in the abdomen which are secondary to acid-peptic irritation.

You are well aware that probably the most severe insult to the peritoneum is to soil it with hydrochloric acid and peptic juice from the stomach, and it is not uncommon to find several liters of serous fluid—virtually pure serum—in the peritoneal cavity when the patient is not seen until 10 or 12 hours after an intestinal perforation. We usually use plasma liberally in replacement therapy for these patients. We treat them in a manner similar to the method Zollinger has suggested for patients with pancreatitis. Of course, we also use saline and some blood, and we choose to wait until the urinary output approaches 30 or 40 cc. per hour before we operate on the patient.

In our hospital, every patient with a perforation of the gastrointestinal tract undergoes operation unless there are compelling reasons contraindicating surgical intervention. A compelling reason would exist, for example, if the patient had been lying in a boarding house for so many days that he was moribund when we first saw him. Any patient with a gastrointestinal perforation whose condition makes him a decent candidate for surgery and who is seen within a reasonable period after perforation (24 to 36 hours) is put in shape quickly and subjected to laparotomy.

Why do we operate on these patients? There are several reasons. We think the spillage from the gastrointestinal tract into the peritoneal cavity is very irritating and induces the severe reaction that results in an outpouring of serous fluid; we believe it is better to clean this up and irrigate the peritoneal cavity thoroughly. Indeed, we rely almost entirely on mechanical irrigation and cleansing of the peritoneal cavity rather than on antibiotics. As Dr. Strobel indicated, the patient just described did not receive systemic antibiotic therapy postoperatively, and this is true of other similar patients in our hospital. By and large they have done very well.

During recent years, suction therapy alone has been tried in cases of perforated duodenal ulcer. I suppose this is all right if you have someone who can stand right at the bedside and aspirate the nasogastric tube to make sure that a good-sized tube stays open and the material is constantly sucked away. But in our hospital the suction apparatus just doesn't work like this, and we don't have the personnel to do that kind of a job; so we believe in early surgical treatment whenever possible. The surgical procedure is very simple; it is a matter of plicating omentum over the perforation. We sew a tab of omentum down over the area of the perforation, taking care not to necrose the tissue or cut off the blood supply as we place the stitches.

Follow-up therapy is important in regard to the need for subsequent resection. We believe that all patients who have a perforation of the duodenum as a complication of the ulcer diathesis should undergo resectional therapy. Why? First, it is obvious that the surgical treatment of the perforation has not corrected the ulcer diathesis. We believe medical therapy is inadequate in the long run to protect this kind of patient from further and continual ulceration in the area of scar tissue which inevitably will form where the patch of omentum was plicated. Therefore, we feel that the patient deserves a subsequent gastric resection of one kind or another. We do not always use the same operative procedure for the ulcer diathesis. The operation is tailored to the patient's mode of life, his habits, and his general body build, and the decision is made individually whether it will be a segmental resection, a 50 per cent resection with vagotomy, a 75 per cent resection as a Billroth II operation, and so on.

Case 2: Gastric Perforation

In 1957 we had five patients with perforated gastric ulcer; in 1958 we had five, and in 1959 we had eight. The mortality rate is

FIGURE 2. Upright abdominal x-ray demonstrating excessive air under both sides of the diaphragm secondary to perforation of a large gastric ulcerating lesion. This amount of free air in the peritoneal cavity indicates the likelihood of perforation in the stomach or the colon.

rather high. Eight of the 18 patients died, but only two of the 12 who were operated on died. This is rather revealing; we have noted that a fair number of these patients come to us in very poor condition, actually almost moribund, after having been in a rest home or nursing home environment with a long delay following perforation. When we have an opportunity to treat these patients relatively early, the result usually is good. The next case concerns a patient with a gastric perforation and raises several points that we can discuss.

DR. STROBEL: A 48 year old mail carrier was admitted to the hospital in April 1959. The night before, he drank some beer and at about 2 o'clock in the morning he awakened with generalized abdominal pain; he vomited twice. The pain was constant. He came to the hospital at about 6 o'clock in the morning. He had never had a similar episode of pain previously, he had never vomited blood or had tarry stools, and he had never had heartburn.

Blood pressure was 140 (systolic) and the pulse rate was 92. The abdomen was boardlike with no bowel sounds. It was tender and moderately distended. Roentgenographic study revealed free air under the diaphragm on both sides (figure 2). The usual preoperative workup was obtained and the patient was given intravenous fluids and plasma.

When his abdomen was opened, at least 200 cc. of gastric contents was found in the peritoneal cavity, including some particles of food. Approximately in the midportion of the stomach, and on the anterior surface, was a perforation ½ cm. in diameter. The upper proximal two-thirds of the stomach was very firm, almost scirrhous, and there was some necrosis in the wall adjacent to the perforation. Multiple biopsy specimens were taken from this area. Because of the extreme rigidity of the stomach, we believed that closing the stomach wall would be hazardous; so a No. 26 Foley catheter with a 30 cc. bag was inserted through the perforation, the wall of the stomach was "snugged up" around it, and then the omentum was wrapped around the catheter, which was then brought out as a gastrostomy tube.

The patient did fairly well in the immediate postoperative period, but nine days later some serous drainage escaped from his wound and he had an evisceration on the ward. He was taken to surgery and this was closed with wire sutures. The patient then recovered without further difficulty.

The biopsy material taken from the stomach wall revealed lymphosarcoma. Since the lesion was high in the stomach, and operative treatment would have had to be in the nature of a total gastrectomy, it was decided that roentgentherapy would be the best treatment, and 3000 r of deep tissue therapy was given over a three week period. Prior to roentgentherapy, a test of gastric acidity revealed 10 degrees of free acid and a total acidity of 63 degrees. Eleven months later, because of some scarring of the stomach observed at follow-up x-ray examination, a "second look" type of procedure was carried out. Multiple biopsy specimens were taken of lymph nodes, and the area of the previous ulcer was excised.

The pathologist was unable to demonstrate tumor in any of the sections. Thus, at this point, as closely as we can tell, the patient is free of tumor.

DR. HITCHCOCK: It has been our experience that patients who have either duodenal perforations or gastric perforations and who get to us in a matter of hours after the catastrophe are not in serious shape. Ordinarily they are not in profound shock. One reads in the textbooks that the first part of this problem is one of *prostration*, and then the patient goes into a period of *reaction* when he may look quite good, and so on. I have never been able to separate this out so clearly. Many of the patients have a very compatible blood pressure, in excess of 100, and with proper supportive therapy they never do go into shock.

I would like to say also that in the management of these perforations of stomach lesions ordinarily it is the benign gastric ulcer that perforates, and when the situation is quite obviously benign, at least grossly, if we can excise the ulcer and close the stomach we will do so. I happened to be involved in this case, and it was the first time I had ever treated such a patient in this manner. It seemed to me that there was a fair chance the man had carcinoma, since the stomach felt quite scirrhous and hard all the way up to the esophagus. It was obvious at this point that if anything were to be done surgically a total gastrectomy would be necessary, because the lesion was fairly high in the stomach. My reasoning was to try and get the patient over the acute episode and take it from there; but in the meantime, of course, we took some tissue for histologic confirmation. This technic of putting a Foley tube into the area of perforation is not new; it is just a matter of performing a gastrostomy. Dragstedt, for example, has used this technic for years in elective surgery, putting a tube in the stomach pouch, wrapping some omentum around it, pulling it up against the abdominal wall, and bringing it to the outside. We did it in this emergency case and it got us over the acute problem nicely.

Whether we should have excised the area or performed a definitive resection and then used x-ray therapy is another problem of management, but it seemed to me that surgical treatment would have required total gastrectomy and I elected not to do this. Roentgentherapy was given and, as Dr. Strobel reported, the results have been good.

Interestingly enough, we have had considerable experience with lymphomas of the stomach in the past year. We have seen six lymphomas of the stomach as primary problems. Five of them were lymphosarcomas and one was Hodgkin's disease. In your community you may have to deal with patients of this kind who are receiving nitrogen mustard therapy, and I want to mention a case from my experience to issue a warning for the future. In a patient with a known lesion in the stomach due to Hodgkin's disease who was receiving nitrogen mustard therapy, there was tumor necrosis after chemotherapy with perforation into the peritoneal cavity.

Case 3: Perforated Appendix

Let us move on to the problem of perforated appendix. In our conferences, as we discuss the problems of appendicitis, some of our general surgeons in the community say that they do not see as much appendicitis as they used to and they wonder if this disease might be less prevalent than formerly. It is difficult to be certain about this, but I believe this kind of problem is managed more by men other than the surgeons, who get only the referred cases.

In from 12 to 25 per cent of the cases of appendicitis that we see at our hospital the appendix is already ruptured at the time of admission. Dr. Strobel will report briefly on a patient who had generalized peritonitis following appendical rupture.

DR. STROBEL: I got to know this patient very well during his long stay in the hospital. He was admitted in July 1959, and stated that he had experienced some abdominal pains for about three days. He vomited occasionally, was unable to eat anything, and had not had a bowel movement since the pain began. When he was admitted to the hospital the pain was generalized, and he said it was most severe in the right lower abdominal quadrant.

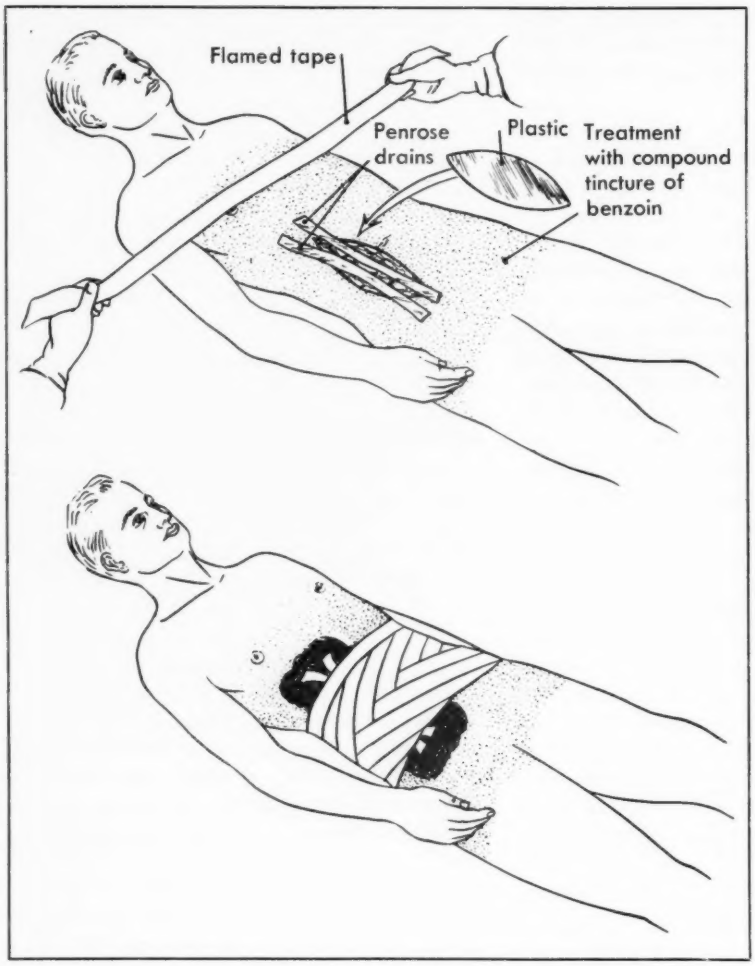


FIGURE 3. Diagram of the procedure permitting total abdominal drainage in cases of diffuse suppurative peritonitis. The patient is placed on his abdomen, preferably on a Foster or Stryker frame, and is maintained in this position of dependent drainage until sepsis is controlled and agglutination of peritoneal surfaces takes place. This is an emergency method of management necessitated by failure of the patient to control an excessive sepsis in the peritoneal cavity.

His abdomen was diffusely tender and rigid, with rebound tenderness throughout. He was perspiring. Blood pressure was 150/90 and pulse rate was 120. Initial laboratory work-up revealed a hemoglobin level of 17 gm., a hematocrit reading of 53 per cent, and a leukocyte count of 17,300. The serum amylase level was 67. We were unable to see any free air in abdominal roentgenograms.

Prior to operation, 3000 cc. of fluid was given over five hours, including 300 cc. of plasma. At operation, a seropurulent material escaped from the abdominal incision and a perforated appendix was found and removed. There was no walling-off of the process. The fascia was closed and the subcutaneous tissue and skin were left open.

Seven days later the patient was not doing well. Bowel function had not returned, he was running a febrile course, and we felt that he had an abscess in the right flank and possibly another in his wound. We opened the old wound and found an abscess between the fascia and peritoneum. We also found a second abscess extending over into the right flank, and a third abscess in the pelvis anterior to the bladder. We put eight drains into the flank and pelvis and left the wound open.

We prevented evisceration with a basket-weave of "flamed adhesive strips" over a plastic drape cut to fit the wound and cover the bowel (figure 3).

Nine days later, bowel function still had not returned; the patient was toxic and vomiting blood. We put him on the hypothermia blanket and brought his temperature down to 90° F. to help control the gastrointestinal hemorrhage. After another five days he was unable to cough well, so we did a tracheostomy. Approximately seven days later we started a Sippy regimen through the nasal tube. A week later we discontinued the hypothermia blanket, and shortly thereafter the patient was given soft food and the tracheostomy tube came out. Another two weeks later a split graft was placed over the granulating tissue covering the bowel, and the patient was dismissed in 10 days.

Three weeks ago the patient came back to the hospital for repair of the ventral hernia and resection of a short segment of small bowel which was closely adherent to the skin. He was dismissed about a week later.

DR. HITCHCOCK: This case raises several points about the management of serious generalized peritonitis. I am convinced that total drainage of the peritoneal cavity is important when the occasion demands it. In some of our patients who have serious gunshot wounds, stab wounds, or generalized peritonitis, and in cases in which we have a problem of sepsis that is uncontrollable, we frequently leave the wound open and treat it as Dr. Strobel indicated. A plastic "apron" protects the intestine from the tape that is to be applied. The skin is prepared right up to the edge of the wound with compound tincture of benzoin so that tape will stick to the edge, and then, using the regular basket-weave type of strapping, the abdomen is "taped" to prevent evisceration. The patient can be placed on his abdomen, and very effective drainage will result. We have used this technic several times in the past year.

The patient represented in figure 4 underwent operation only today for repair of a ventral hernia subsequent to this kind of management. A split graft was placed on the area of granulation tissue about four months ago before he left the hospital. He had sustained a serious gunshot wound. The whole pelvis was torn up, and a colostomy was necessary initially. This method of management fulfills the cardinal principle of adequate drainage of an area of sepsis. Many other methods for draining a septic abdomen have been used in our clinic and have proved unsuccessful; I refer to the use of sumps or simple placement of Penrose drains into dependent cavities.

FIGURE 4. Postrecovery hernia in a patient with a severe gunshot wound of the abdomen and subsequent generalized suppurative peritonitis. Treatment was instituted as diagramed in figure 3. Such hernias can be successfully repaired after complete recovery from the major illness.

Stress Ulceration

It is important to watch the patient's overall reaction in terms of stress ulcer. This is another area where we have had a good experience, the problem of stress bleeding or stress ulceration of the stomach and duodenum. A fairly high percentage of our patients who come in with serious traumatic injury or with very severe peritonitis subse-

quently bleed from the upper gastrointestinal tract. One good way to treat these patients is the local gastric cooling method, about which you undoubtedly will hear more during this continuation course. We have not used it at our hospital, not because we have not wanted to but because we have not had the necessary special equipment. So we have used general body hypothermia. We have carried some of these patients for as long as seven and eight days at temperatures of 86 and 88° F., and there are only a few problems that need emphasis. We always perform a tracheostomy, since the patients do not cough properly. We watch the fluid-electrolyte balance particularly carefully; overhydration and waterlogging can occur rather easily, since these patients do not lose water in the same degree as does a normothermic patient.

Other Gastrointestinal Perforations

As far as the rest of the gastrointestinal tract is concerned, we have little to present that would be new and interesting. Diverticulitis in our hospital has been mainly a problem of local abscess and the necessity for an occasional deviating colostomy and drainage of the abscess. I cannot recall, in recent years, seeing a case of generalized peritonitis due to a perforation of a diverticulum.

Crohn's disease or regional ileitis is very rare in our hospital. In addition, we see few cases of ulcerative colitis; usually in this disease the patient suffers from the ravages of the disease over a prolonged period rather than from perforation. Meckel's diverticulum, in our experience, ordinarily does not perforate. We have had the usual experience of finding gastric mucosa or pancreatic tissue in Meckel's diverticula but we have had no trouble from the standpoint of perforation.

Discussion

QUESTION: What antibiotic therapy, if any, did you use in case 3?

DR. HITCHCOCK: Initially we gave CHLOROMYCETIN® until we had the results of cultures. *Escherichia coli* was present deep in the wound. After about 10 days the organisms became resistant, and the patient was switched to TERRAMYCIN® therapy for about another seven days. After that we discontinued antibiotics since we had provided adequate drainage and didn't believe the antibiotics were helping. I think the antibiotics probably did benefit the patient initially, but getting the abdomen adequately drained is what really brought him around.

I don't want you to think that all our patients go to this extreme, even with generalized peritonitis. We had a 22 year old man recently who entered the hospital on a Wednesday with an obvious severe acute peritoneal problem which we diagnosed as perforated appendix with generalized peritonitis. He told us he absolutely would not permit us to operate on him because he was scheduled to be married the following Saturday and *nothing* was going to interfere with his wedding. We finally called the young man's fiancée and she convinced him he had better undergo operation. This young fellow had his appendix out, the peritoneal cavity irrigated thoroughly, and the wound closed. By Saturday he was really looking like a fit bridegroom and, indeed, he was discharged from the hospital a week later and did beautifully.

I do not know how anyone can be sure which patient is going to present the more serious problem as described in case 3 and which one will get along as this latter young man did. We ordinarily do not close the skin and subcutaneous tissue in cases of frank intraabdominal sepsis because we have learned from experience that an abscess frequently will develop in the subcutaneous fat. We close the fascia and leave the wound open, and perform a secondary closure later.

I am a firm believer in mechanical cleansing. I believe in it as thoroughly for the peritoneal cavity as I do in washing my hands before surgery. On occasion, I have used as much as 7 or 8 liters of saline to thoroughly cleanse a peritoneal cavity that has been diffusely soiled from one type of spillage or another. It seems to me that this has been very beneficial in our hospital.

QUESTION: If a female has a localized, well-controlled abscess in the pelvis, how do you drain it?

DR. HITCHCOCK: We do not drain through the perineum or through the rectum or through the vagina; we drain through the lower quadrant, preferably the left lower abdominal quadrant. We do not irrigate widely in this kind of localized abscess.

QUESTION: Do you have any eviscerations in these instances in which you do not close the abdomen?

DR. HITCHCOCK: These *are* eviscerations in the true sense of the word. The wounds are open. But if you leave them alone with strapping as we have demonstrated, the patient gains control of the infection after six or seven days and begins to form granulation tissue over the bowel. Peristalsis returns and the bowel regains normal function. The resulting hernias should be repaired later. In these extreme cases in which purulent material would be retained within the peritoneal cavity, this kind of maneuver, drastic as it seems, can be lifesaving. These patients pose tremendous problems in nursing and daily ward care. I felt it was worthwhile to talk to you about something that is not quite so standardized and is more of a challenge.

MEETINGS *and Postgraduate Courses*

AMERICAN ACADEMY OF PEDIATRICS, WASHINGTON, D.C.: Spring session to be held at the Sheraton-Park Hotel, April 10-12. For further information, write to: Executive Office of the Academy, 1801 Hinman Avenue, Evanston, Illinois.

AMERICAN PSYCHOSOMATIC SOCIETY, ATLANTIC CITY: Eighteenth annual meeting to be held at the Chalfonte-Haddon Hall Hotel, April 28-30. For further information, write to: American Psychosomatic Society, 265 Nassau Road, Roosevelt, New York.

INTERNATIONAL ACADEMY OF PROCTOLOGY, CHICAGO: Thirteenth annual convention to be held at the Drake Hotel, April 8-13. For further information, write to: Dr. Alfred J. Cantor, Executive Officer, International Academy of Proctology, 147-41 Sanford Avenue, Flushing 55, New York.

INTERNATIONAL COLLEGE OF SURGEONS: The twenty-sixth annual congress of the North American Federation will be held at the Palmer House, Chicago, May 14-18. Sectional meetings will be held as follows:

French section, Vittel, France, June 16-18
New England region, Chatham, Massachusetts, July 1-4
Western section, San Francisco, November 19-22

For further information, write to: International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

MOUNT SINAI HOSPITAL OF GREATER MIAMI, MIAMI BEACH: Eleventh annual postgraduate seminar to be held at the Seville Hotel, May 18-20. For further information, write to: Dr. Mortimer D. Abrashkin, Meridian Medical Center, 1680 Meridian Avenue, Miami Beach 39.

NEW YORK UNIVERSITY POST-GRADUATE MEDICAL SCHOOL, NEW YORK: Postgraduate course in gynecologic endocrinology to be held April 17-21. For further information, write to: Office of the Associate Dean, New York University Post-Graduate Medical School, 550 First Avenue, New York 16.

UNIVERSITY OF CALIFORNIA MEDICAL CENTER, SAN FRANCISCO: Postgraduate courses to be held in 1961:

Evening lectures in medicine, Eden Hospital, Castro Valley, April 4-May 23
Laboratory investigation of endocrine disorders, April 7-9
General surgery, April 13-15
Ear, nose and throat, May 11-13
Proctology, May 18-19
Water, salts and steroids, May 25-27
Ophthalmology, June 1-3
Basic course in electrocardiography for the general physician, June 9-10
Psychiatry for the general practitioner, June 15-17
Cerebral palsy, June 29-30

For further information, write to: Dr. Seymour M. Farber, Assistant Dean in Charge of Continuing Education, University of California Medical Center, San Francisco 22.

Lectures on the substrates of behavior to be held in the Medical Sciences Auditorium:

Hypothalamic correlates of behavior, April 18
Neurons, notions and neuroses, May 16

For further information, write to: Advisory Committee, Interdisciplinary Program, University of California Medical Center, San Francisco 22.

UNIVERSITY OF LOUISVILLE SCHOOL OF MEDICINE, LOUISVILLE: Postgraduate course in pediatrics to be held on Tuesdays, April 4-May 23, at the Children's Hospital. For further information, write to: Dr. Friedrich Hertle, Executive Director, Postgraduate Medical Education Office, 104 West Chestnut Street, Louisville 2.

UNIVERSITY OF MINNESOTA, MINNEAPOLIS: The course on surgery for surgeons, to be presented at the Center for Continuation Study, will be held May 11-13 rather than May 11-12, as previously announced. For further information, write to: Director, Department of Continuation Medical Education, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.

Horizons in Abdominal Surgery

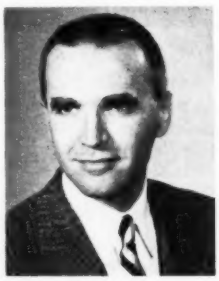
RICHARD C. LILLEHEI, JERROLD K. LONGERBEAM, BERNARD GOOTT, SADEK HILAL AND EDMOND YUNIS

University of Minnesota Medical School, Minneapolis

Behold, the former things are come to pass, and new things do I declare: before they spring forth I tell you of them.

Isaiah 42:9

PERHAPS it is safer to give a prophetic talk than almost any other kind, for if the speaker's remarks seem unreasonable to the audience at the time he may in return merely picture his auditors as shortsighted realists without creative thought. Moreover, if time later proves (as it often does) that the speaker was indeed utterly wrong in his predictions, few will remember it. On the other hand, if by some remote chance the would-be seer blunders into saying anything that happens to come true in the years ahead, he will surely call it to the attention of his colleagues (if he is still alive) and hence will be labeled a man ahead of his time.



RICHARD C. LILLEHEI

Having fortified myself with such specious reasoning, I would like to present work from the laboratory concerning transplantation of visceral organs—procedures which will, I believe, become commonplace in our lifetime.

The Decade of Organ Transplantation

If the 1950s could be labeled the decade of open heart surgery, the 1960s may well deserve some day the title the decade of organ transplantation. To deserve this appellation, numerous immunologic, physiologic and technical problems must first be solved. The present study describes small efforts made toward achieving these goals.

You may ask what surgeons are doing in a field where the basic problems are primarily chemical or immunologic in nature. Research

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FIGURE 1. Charles Claude Guthrie, author of "Blood-Vessel Surgery and Its Applications," published in 1912.

FIGURE 2. Two-headed dog created by Dr. Guthrie. The transplanted head is upside down and inferior to the host's head.

From Guthrie, C.C.: Blood-Vessel Surgery and Its Applications.

of late years has lost respect for narrow specialty boundaries, and the future of medicine lies certainly in directions other than further multiplication and refinements of specialties. I believe we are on the verge of that state described by Galdston[1] wherein "the emergent unifying principles in the biologic sciences promise to make of medicine a consistent and meaningful discipline, compact in principle and pervasive in application"—and, we hope, with fewer narrow specialties.

History of Transplantation

In surveying the development of transplantation, which is entwined with if not identical with the development of vascular surgery, the accomplishments of Alexis Carrel[2] immediately come to mind. Less well known but equally deserving of recognition for his contributions in this field is Charles Guthrie (figure 1). This remarkable physiologist, now an octogenarian, is the author of a book published in 1912, "Blood-Vessel Surgery and Its Applications,"[3] which described his investigations in the transplantation of organs and in vascular surgery. He was able to transplant kidneys, ovaries, testicles, thyroids, parathyroids, lungs, hearts and thighs. And, incidentally, despite the peremptory claims of the Russians, Dr. Guthrie first successfully transplanted a dog's head to make a two-headed dog in 1908, several decades before the Russian rediscovery (figure 2).

One can see from the long list of Guthrie's accomplishments that few choices of organs were left. Previous studies on the nature of irreversible shock had focused our attention on the many unknowns surrounding the physiologic response of the small bowel to varying degrees of ischemia and the disturbances resulting from such ischemia.[4-6] It seemed to us that experimentalists had perhaps neglected the bowel for more glamorous and less aromatic organs such as the heart.

Response of the Small Bowel to Ischemia in Vivo

Will the bowel withstand the prolonged ischemia necessarily attendant to any transplantation procedure? What is the difference in response to partial rather than complete occlusion of the small bowel's circulation? What is the influence of temperature on the effects of ischemia? These are vital questions, since the metabolic rate of the small bowel mucosa exceeds that of all other organs.[7] The existing literature on this subject is incomplete and reported results are often contradictory in nature.[8-11] Thus our initial task was to determine in vivo the ability of the bowel to survive complete or partial interruption of its circulation.

Methods—All experiments in this presentation were carried out on adult mongrel dogs of either sex which were anesthetized with sodium PENTOTHAL®. Aseptic technic was used for all procedures. An autopsy was conducted on all dogs that died as well as on

those that survived and were then sacrificed at varying periods following the experiments.

In previous studies we noted that plasma volume loss and a concomitant hematocrit increase were directly proportional to the degree of intestinal ischemia.[4-6] That is, with increasing severity of the intestinal ischemia, increasing amounts of plasma were lost into the ischemic bowel. Moreover, in the dog, plasma hemoglobin increased significantly in those dogs which subsequently died of hemorrhagic necrosis of the bowel as a result of ischemia which exceeded critical limits.[5] These three plasma determinations also proved to be accurate harbingers of the ultimate fate of the bowels of dogs subjected to varying degrees of ischemia in the experiments to be described.

The plasma volume was measured using T-1824 and a micromethod described previously.[4] The hematocrit determinations were made in Wintrobe tubes, and plasma hemoglobin was measured by the method of Flink and Watson.[12]

Partial and complete interruption of circulation in vivo—The superior mesenteric artery was occluded by clamping just distal to its origin from the aorta. To occlude all collateral circulation to the small bowel as well, the following procedure was used. At a point on the duodenum just distal to the pancreas, the duodenal mesentery was divided between clamps down to the superior mesenteric vein. Similarly at a point in the ileal mesentery just proximal to the ileocecal valve, the mesentery was also divided between clamps down to the superior mesenteric vessels. A small communicating artery along the antimesenteric border of the terminal ileum joining the inferior mesenteric arterial system with the superior mesenteric system was also divided and ligated. Finally, to occlude all intramural collateral circulation, noncrushing clamps were placed across the duodenum and terminal ileum at the points where the mesentery had been divided (figure 3).

Hypothermia of the small bowel in vivo—To produce localized hypothermia of the small bowel, the following procedure was used. Arterial circulation to the small bowel was occluded completely as already described. In addition, the superior mesenteric vein was clamped distal to the entrance of the inferior mesenteric vein. The superior mesenteric vessels were both cannulated with plastic catheters distal to the vascular clamps, and saline at 5° C. was pumped into the arterial catheter and allowed to drain out from the venous catheter (figure 4). With this procedure it was possible to cool the small bowel to 5° C. in a few minutes, at which temperature it would remain for prolonged periods without the need for continuous perfusion. Heat lamps and heating pads kept the dog's general body temperature above 35° C.

At the end of the period of occlusion, the catheters were removed from the superior mesenteric vessels and the cannulation sites in these vessels were carefully repaired with 6-0 silk. The arterial clamps were then removed from these vessels, along with the noncrushing clamps on the duodenum and terminal ileum. To prevent precipitous drops in the body temperature of the dog as circulation was resumed through the cold bowel, the peritoneal cavity was flooded with warm saline (40 to 42° C.). This measure prevented any great change in body temperature during the period of rewarming of the bowel. The abdominal wound was closed and the dog was allowed to awaken. No heparin was used in any of these experiments to prevent thrombosis during the period of circulatory arrest of the bowel.

Results—Table 1 presents a brief summary of the results of these experiments. When the superior mesenteric artery alone was clamped for three to three and one-half hours, followed by removal of the clamp on the artery and closure of the abdominal wound, most of the dogs survived. However, when the period of occlusion of the superior mesenteric artery alone was increased to five hours, only one of 10 dogs survived. The rest died of hemorrhagic necrosis of the bowel. Sterilization of the bowel by giving neomycin and SULFASUXIDINE® orally for five days prior to an experiment so that stool cultures were sterile on the day of an experiment also did not provide protection against a five hour period of occlusion of the superior mesenteric artery.

In contrast to the favorable results of occlusion of the superior mesenteric artery alone for three to three and one-half hours, when all collateral blood supply was also interrupted for this same period of time only one dog survived; the others died of necrosis of the small bowel. In order to get survival of the small bowel when all collaterals were divided, it was necessary to reduce the period of occlusion of the superior mesenteric artery to two hours. In these dogs in which all arterial circulation to the bowel was stopped, the temperature of the bowel dropped quite promptly to room temperature (25 to 28° C.), and this no doubt favorably influenced survival. Further evidence of the favorable effect of lowered temperature is the results when the bowel was cooled to 5° C. All but one of these dogs survived a five hour occlusion of the superior mesenteric artery as well as division of all collaterals without any subsequent damage to the small bowel.

Physiologic effects of intestinal ischemia—The effects of the intestinal ischemia on plasma volume and hematocrit paralleled the results obtained in previous studies of hemorrhagic and endotoxin shock. That is, in the present experiments, the more prolonged and more complete the interruption of the circulation to the small bowel, the greater was the plasma loss into the small bowel upon resumption of the circulation to the bowel (figure 5). Moreover, in those dogs in which the intestinal ischemia was intense enough to cause ultimate death from intestinal necrosis, the plasma hemoglobin invariably rose to high levels before death, indicating that hemorrhagic necrosis of the intestine had occurred as a result of the ischemia and that the animals would soon die (figure 6). There is no evidence that these elevated levels of plasma hemoglobin are lethal in themselves, but they merely indicate that the integrity of the intestinal mucosa has been damaged and that blood is accumulating within the intestinal lumen. There the blood is hemolyzed and again reabsorbed into the circulation through the damaged mucosa, doubtless along with other toxic products resulting from mucosal necrosis.

It is noteworthy that irreversible hemorrhagic shock with its inevitable hemorrhagic bowel necrosis occurs only after four and one-half to five hours of profound oligemic hypotension followed by retransfusion. Similarly, in the present experiments, the characteristic hemorrhagic necrosis of the intestine occurred only after about five hours of superior mesenteric occlusion followed by release of the occlusion. If the superior mesenteric occlusion is maintained permanently, however, along with division of collaterals, the characteristic plasma findings described previously do not occur until much later and survival also is prolonged, although death nevertheless occurs eventually. This is because early fluid losses into the ischemic bowel are minimized and the toxic products of intestinal necrosis are not washed directly into the general circulation by release of the occlusion but are denied access to the circulation until they have permeated through the bowel wall and then have been reabsorbed from the peritoneal cavity.

Another correlation between death due to superior mesenteric arterial occlusion and death due to irreversible hemorrhagic or endotoxin shock concerns blood flow to the bowel. Normal arterial inflow into the small bowel averages about 10 to 15 ml. per kilogram per minute in the dog, but during prolonged shock this inevitably drops to less than 1 ml. per kilogram per minute. Collateral blood flow into the small bowel in which the superior mesenteric artery has been occluded also averages less than 1 ml. per kilogram per minute.[13] In both these conditions this small residual flow is able to sustain the viability of the small bowel of the dog at normal body temperature if the period is not too prolonged, as evidenced by our experience that the dogs regularly recover if the period of hemorrhagic shock is three hours or less or if the period of occlusion of the superior mesenteric artery is three hours or less.

Significance of these studies—Our objective in these experiments was to establish the tolerable limits of ischemia in the small bowel in vivo, both as to total and partial circulatory arrest and at varying temperatures. In addition, the experience gained in carrying out the technical aspects of the experiments showed

TABLE 1

RESPONSE OF THE SMALL BOWEL TO ISCHEMIA IN VIVO

GROUP	NUMBER OF DOGS	TYPE OF OCCLUSION	DURATION OF OCCLUSION (HOURS)	MAXIMAL VALUES WITHIN EIGHT HOURS FOLLOWING RELEASE OF OCCLUSION*			SURVIVORS (48 HOURS OR MORE)
				Plasma volume loss (per cent)	*Hematocrit increase (per cent)*	*Plasma hemoglobin increase (milligrams per cent)†*	
1	10	Superior mesenteric artery (S.M.A.) only	3 to 3½	24.9 ± 4.3	25.1 ± 6.93	25.2 ± 9.7	7
2	10	S.M.A. only	5	44.9 ± 12	30.9 ± 6.9	108 ± 49	1
3	5	S.M.A. only; pretreatment with neomycin-Sulfasuxidine for five days	5	34.7 ± 11	27.4 ± 7.4	97.2 ± 31.6	0
4	10	S.M.A. and all collaterals	3 to 3½	37.7 ± 8.8	30.1 ± 5.1	75 ± 20.2	1
5	10	S.M.A. and all collaterals‡	2	16.3 ± 7.9	16.4 ± 7.7	20.4 ± 10.8	8
6	10	S.M.A. and all collaterals; intestinal hypothermia to 5° C.	5	26.5 ± 9.9	28.1 ± 8.7	18.6 ± 8.9	9

*Mean values with standard deviations.

†Normal values in dogs, 5 to 10 mg. per cent.

‡Peritoneal cavity left open and small bowel allowed to cool to room temperature (25 to 28° C.).

us that the anatomic status of the superior mesenteric artery and vein was such that one could remove almost the entire small bowel, save for a few centimeters of duodenum, preserving its vasculature in such a way that a single arterial and venous anastomosis would completely revascularize the bowel (figure 7).

The results of the in vivo experiments also indicated that the bowel could withstand at least two hours of total circulatory arrest by merely allowing it to cool to room temperature. There seemed no reason, then, that we could not remove the bowel completely from the peritoneal cavity if we reconstituted circulation by the two hour time limit. Moreover, if by some means we lowered the temperature of the resected bowel to 5° C., there appeared to be no need for any circulation for at least five hours. The question remained whether or not this removed bowel would regain normal function and survive indefinitely following reestablishment of circulation and continuity with the remainder of the digestive tract, in the face of complete severance of all nervous and lymphatic tissues which could not be rejoined.

Removal of the Small Bowel With in Vitro Preservation Followed by Replacement[14]

Operative procedure—The dogs were prepared in a manner similar to that already described, and control determinations of plasma volume, hematocrit and plasma hemoglobin were obtained. The animals were then anesthetized with sodium Pentothal.

The abdominal cavity was opened widely in the midline. The ligamentous attachments of the distal duodenum and proximal jejunum to the colon and the dorsal parietal peritoneum were first divided. Then, working along the right side of the ileocecal mesentery, the superior mesenteric vein was exposed just proximal to the confluence of the numerous tributaries from the small bowel. Following this, the dissection was continued on the left side of the ileocecal mesentery, exposing the superior mesenteric artery. This was followed by careful dissection, division and ligation of all nervous and lymphatic tissue around the superior mesenteric artery, being careful to preserve all branches of this artery. All tissue

surrounding the superior mesenteric vein was likewise divided, carefully preserving all tributaries and taking special care with the inferior mesenteric vein; this vein, although small, drains almost the entire colon in the dog, and accidental division of it often caused a venous infarction of the colon necessitating its removal. The duodenum was divided about 5 to 8 cm. from the pylorus in order to preserve the bile and pancreatic ducts opening into the duodenum, and the duodenal mesentery was then divided down to the superior mesenteric vessels. The ileum was divided about 1 cm. from the ileocecal valve and its mesentery divided down to the superior mesenteric vessels. This left the small bowel pedicled on the superior mesenteric vessels. These vessels were clamped with Kapp-Beck vascular clamps and divided. This allowed us to lift the entire small bowel from the peritoneal cavity leaving only the colon, stomach and a few centimeters of duodenum (figures 8, 9 and 10).

The removed bowel was placed in a sterile towel where it was kept for periods of one to two hours at room temperature (25 to 28° C.). During this time the abdominal cavity of the dog was either left open or closed temporarily with towel clips. At the time appointed for replacement, the abdominal cavity was reopened and the bowel was placed back in the peritoneal cavity, care being taken to place the bowel in its normal relationships to the remaining short segment of duodenum and the colon. The arterial anastomosis was done first, using an over-and-over suture of 6-0 arterial silk, and then the venous anastomosis was made. In anastomosing these vessels, whose internal diameter usually was no more than 3 mm. (the arteries often less than this), we found that a simple over-and-over continuous suture gave the best results (figure 11).

After anastomosing these vessels, the distal duodenum was joined to the proximal duodenum by a one-layer closed anastomosis with 5-0 silk over Wangensteen aseptic clamps. The terminal ileum was joined to the colon by the same technic, after resecting the cecum to facilitate the anastomosis. The gaps in the mesentery of the anastomosed bowel were closed and the root of the mesentery was sutured to the dorsal parietal peritoneum between the aorta and inferior vena cava to give support to the bowel and prevent torsion of the mesentery around the superior mesenteric vessels (figure 12). The abdominal cavity was closed after a copious rinsing of the peritoneal cavity with sterile saline.

A second determination of plasma volume, hematocrit and plasma hemoglobin was obtained about two hours after resumption of superior mesenteric circulation, and measurements were made again at four hours and 24 hours following replacement of the bowel.

Prolonged preservation of the small bowel by in vitro cooling to 5° C.—In vivo studies had shown that the small bowel could survive complete interruption of its circulation for as long as five hours if cooled to 5° C. There seemed no reason, then, that it could not also survive a similar period in vitro if cooled to a similar temperature. Accordingly, in other dogs the small bowel was removed in the manner described and cooled by placing the resected bowel in a sterile plastic bag and immersing it in a beaker of saline previously cooled to 5° C. with ice and salt (figure 13). This procedure cooled the bowel almost immediately to 5° C. The beaker containing the bowel was then placed in a refrigerator where the 5° C. temperature could be maintained indefinitely (figure 14). About five hours later the bowel was taken from the refrigerator and returned to the peritoneal cavity of the dog, where its continuity was restored as described (figure 15).

Results of replacement experiments—In all the experiments, whether the bowel was held in vitro for only two hours at room temperature or for five hours at 5° C., the bowel promptly recovered its normal color and peristalsis following re-establishment of the circulation. Depending on the period of time the bowel had been held in vitro, varying degrees of edema of the bowel wall appeared, but there was no evidence of any loss of viability of the bowel. While the bowel gave every evidence of surviving the procedure, at first it was difficult to obtain survival of the dog following the procedure. Death was most often due to leakage from intestinal anastomoses or to

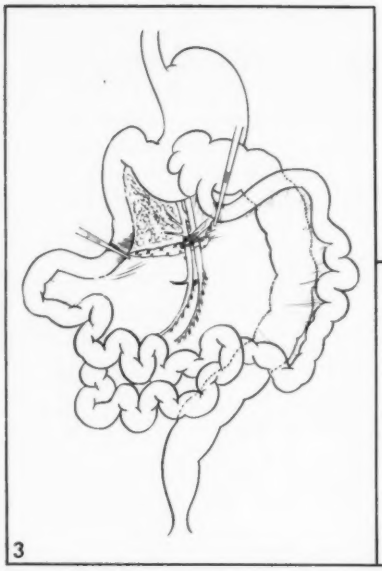
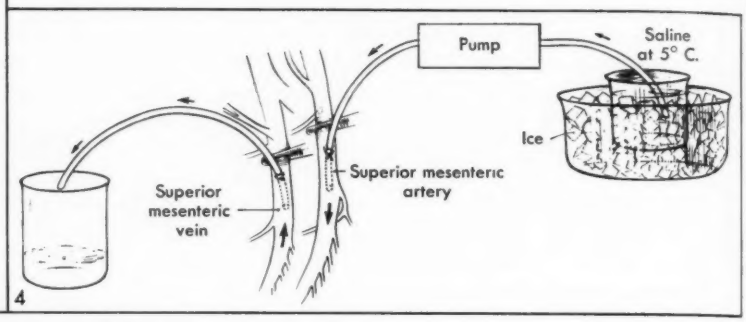


FIGURE 3. Occlusion of superior mesenteric vessels and all collateral blood supply to the small bowel.

FIGURE 4. In vivo cooling of the small bowel.



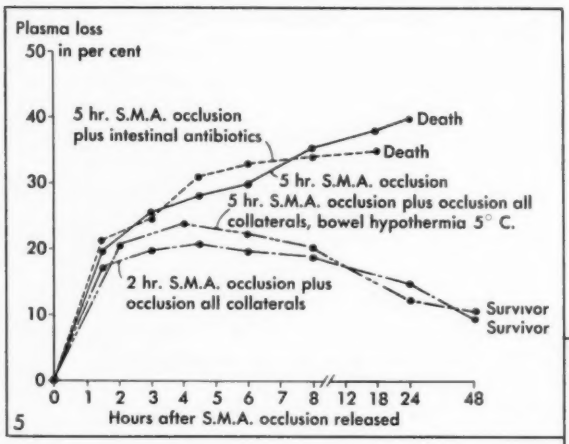
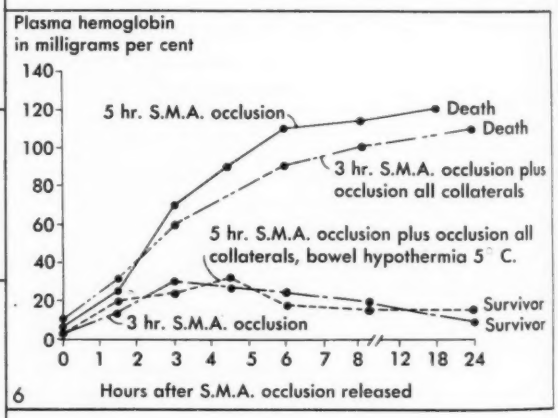


FIGURE 5. Plasma loss in typical experiments.

FIGURE 6. Plasma hemoglobin in typical experiments.



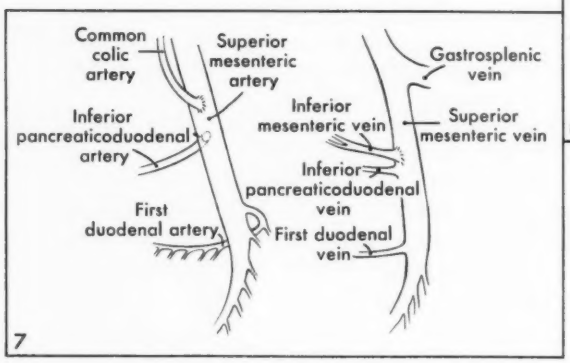


FIGURE 7. Anatomy of the superior mesenteric vessels in the dog.

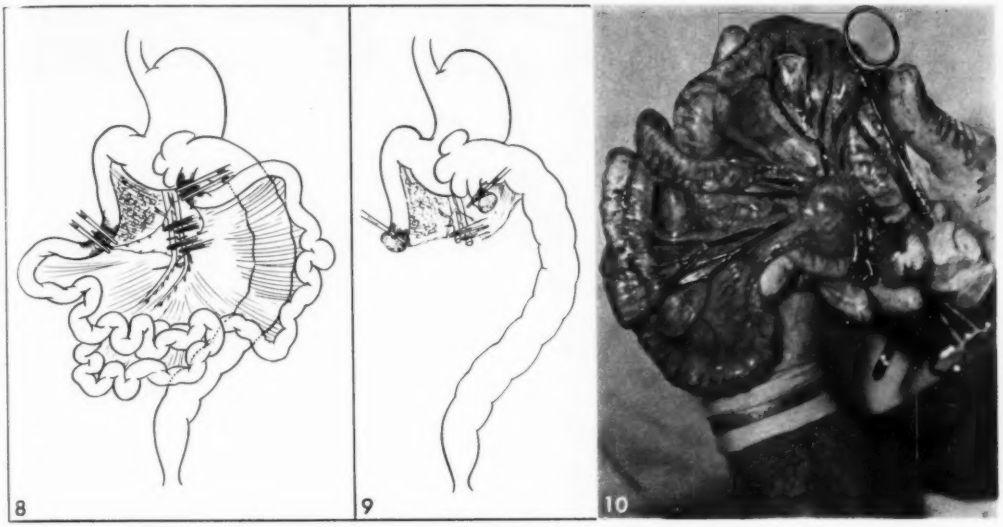


FIGURE 8. The mesentery has been divided and clamps are in place preparatory to dividing the bowel and the superior mesenteric vessels and removing the small bowel.

FIGURE 9. Entire small bowel except for a few centimeters of duodenum has been removed.

FIGURE 10. In vitro appearance of the resected small bowel.

pneumonia. Surprisingly, we had little trouble with thromboses of the anastomosed superior mesenteric artery or vein despite the fact that heparin was not used. After much trial and error we were ultimately able to carry out the replacement of the small bowel with a low initial mortality and also obtain long-term survivors.

In table 2 are the results of 20 consecutive experiments in which the majority of the dogs were long-term survivors. The severity of the edema in the removed bowels is mirrored by the degree of plasma volume loss following replacement of the bowel. The dogs in which the bowel was held in vitro for periods up to five hours lost more than a third of their

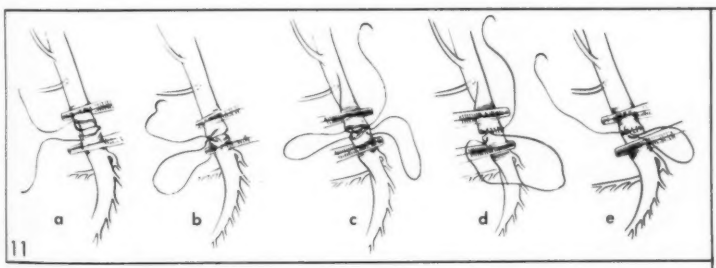


FIGURE 11. Anastomosis of superior mesenteric vessels.

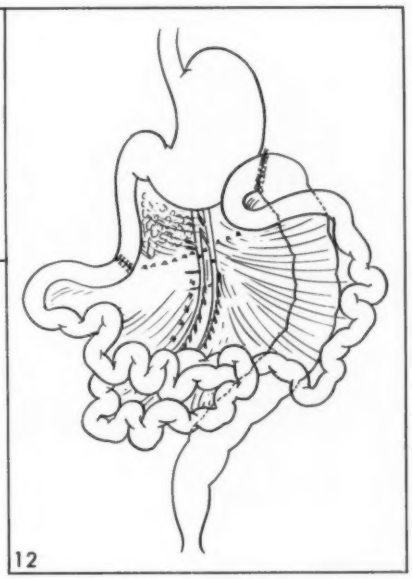


FIGURE 12. Replacement of the small bowel as an autograft. After anastomosis of the bowel to the duodenum above and the colon below and rejoining the superior mesenteric vessels, the root of the mesentery is sutured to the parietal peritoneum to prevent torsion of the bowel.

plasma volume, while dogs in which the bowel was replaced after two hours showed correspondingly less plasma loss. An interesting finding was that although plasma volume losses were large, indicating quite severe intestinal ischemia on the basis of our previous studies, the plasma hemoglobin did not rise to the levels indicative of critical intestinal ischemia with resultant intestinal necrosis. This fact agreed with the observed appearance of the bowel following replacement, for although it was edematous it regained its normal color and showed no signs of loss of viability and was normal when examined later at autopsy or when the dogs were sacrificed.

After determining the plasma changes in these dogs after surgery, we gave intravenous fluids, usually 300 to 600 ml. of normal saline in 5 per cent dextrose. The dogs were maintained on intravenous fluids for three more days before oral intake was allowed.

Nutrition of survivors—The period of recovery of dogs in these experiments could be divided into three stages. During the first week the hematocrit dropped gradually, concomitantly with a gradual return of the plasma volume to normal or above normal levels. This increase in plasma volume apparently was related to resorption of the edema fluid from the bowel wall, for the bowel no longer was edematous and appeared normal when selected animals were re-explored and then sacrificed during this initial period. Almost all dogs also had diarrhea during this first week. By the second week the dogs showed increasing vigor and the stools appeared more normal. At this stage the dogs ate solid foods without difficulty although they continued to lose weight. By the third week the dogs had reached the final recovery stage, and from this period on they gained weight rapidly, usually regaining their preoperative weight by six to eight weeks (figure 16). By this time the stools were normal and ingested fats were handled without excessive loss in the stool. This latter fact indicated that either mesenteric lymphatics had regenerated sufficiently to enable fat absorption to proceed in a normal manner or the fat absorption was being accomplished by some other means. To answer the question of how fats were being absorbed in dogs with autografts of small bowel, the following investigation was made.

Mesenteric lymphatic regeneration[15]—In this phase of the study we selected six dogs in which the small bowel had been removed and cooled to 5° C. and then replaced. It should be noted again that no attempt was made to re-establish lymphatic connections at the time the small bowel was replaced. The six dogs selected for this study were re-explored one week, two weeks, and one, three, four and 12 months, respectively, following placement of the autograft. Two methods were used to outline any regenerated lymphatics which may have re-established connections between the autografted small bowel and the central lymphatic system, thereby accounting for the normal fat absorption. In the first method we injected sky-blue dye into a lymph node or lymph channel of the autografted small bowel. In the second we utilized a radiopaque dye (RENOGRAFIN®); it also was injected into a lymph node of the autograft.

Results of lymphatic visualization—The results of this phase of the study are seen in figure 17. When 0.5 ml. of sky-blue dye was injected into the nodes of the mesentery of the autografted bowel, gentle massage resulted in rapid appearance of the dye across the line of resection of the mesentery. Within 15 minutes the lymphatics around the portal vein and the thoracic duct were outlined by the blue dye. This could only occur if lymphatic regeneration had re-established connections between the lymphatics of the autograft and the central lymphatic system. Radiographic studies confirmed what had been seen with the use of the sky-blue dye. Following injection of Renografin into the lymph system of the autografted bowel, the radiopaque material could be seen in lymphatics around the portal vein and in the thoracic duct when x-rays were taken (figure 18).

The lymphatic regeneration could be demonstrated as early as two weeks after placement of the autograft; and the longer the interval after placement, the more completely the lymphatics had regenerated. The early appearance of these new lymphatics explained

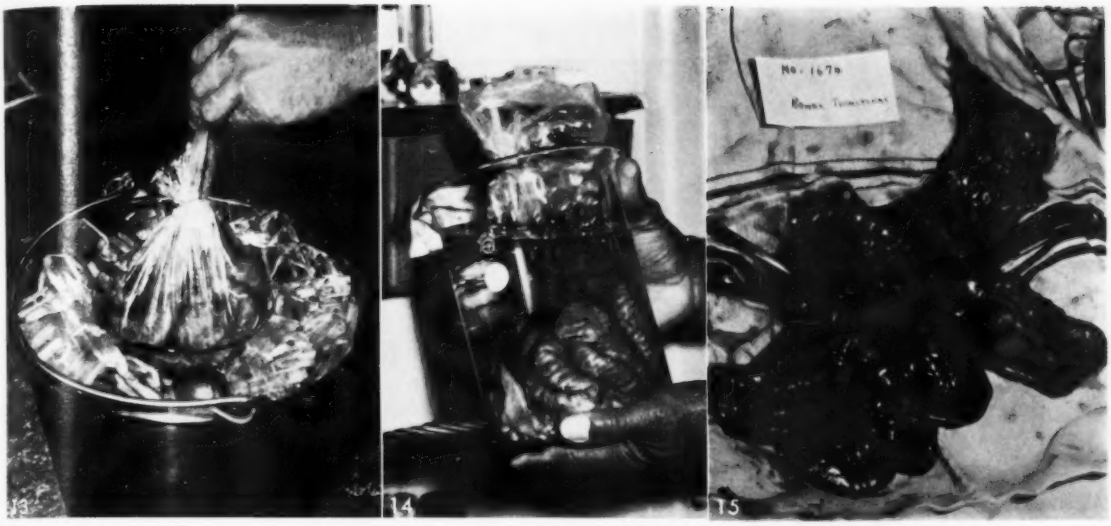


FIGURE 13. The small bowel has been placed in a sterile plastic bag and immersed in saline cooled to 5° C.

FIGURE 14. The bowel, cooled to 5° C., is placed in the refrigerator to maintain this temperature for five hours.

FIGURE 15. Normal appearance of small bowel which was stored in vitro for five hours at 5° C. and then replaced, with re-establishment of circulation and intestinal continuity.

why these dogs with an almost total autograft of the small bowel were able to handle fats in a normal fashion after two weeks and were thus able to regain a normal state of health and survive indefinitely. The oldest survivor has now lived two years.

These results, demonstrating prompt lymphatic regrowth sufficient to maintain normal nutrition, and knowledge gained from our previous experiments indicating that anastomoses of the superior mesenteric vessels will remain patent may have the immediate goal of stimulating surgeons to do more aggressive operations for malignancies involving the superior mesenteric vessels and adjacent tissues without fear of late thrombosis of these vessels or of nutritional problems due to faulty fat absorption. The long-range goal is to be able to replace resected bowel with homografts of bowel. In the latter regard, the ease with which the small bowel could be removed and replaced when desired prompted us to study homografts of the small bowel.

Homografts of the Small Bowel[16]

Most homograft studies have concerned the fate of skin or kidney transplants in animals or man. While the immune mechanisms involved in homograft rejection are doubtless similar if not identical for all organ transplants, the study of the fate of other organ transplants besides skin or kidney might provide clues to the physiologic mystery of homograft rejection. The bowel appears to be a particularly appropriate organ to study because its rich bacterial flora and the antigens

FIGURE 16. This dog had an autograft of the small bowel six weeks before this photograph was made. The dog has regained its preoperative weight.

FIGURE 17. Sky-blue dye visible in lymphatics around portal vein shortly after injection of the dye into a lymph channel of the autografted bowel. This dog was re-explored one month after autotransplantation of the small bowel was performed.

FIGURE 18. Renografin visible around portal vein and in thoracic duct 30 minutes after being injected into a lymph channel of a small bowel autograft.

associated with this flora might profoundly alter, either favorably or unfavorably, the rejection phenomenon.

The procedure of removing the bowel was the same as already outlined. Two mongrel dogs of similar build and weight were operated on simultaneously. The small bowel of each animal was removed and transplanted to the other animal, with restoration of the vascular and intestinal continuity of the homografted bowel in the manner described in the foregoing section. Measurements of hematocrit, plasma hemoglobin, white blood cells and plasma volume were made daily.

Results—Table 3 details the fate of the dogs in these experiments. Most of the dogs which died in the first two or three days were victims of technical errors on our part, but as we got further along in the series we found little to explain the deaths of most of the dogs. This was particularly true of the animals which died between the sixth and the eighth day.

A word is needed here about the clinical picture of the dogs with homografts of small bowel. The dogs were supported with parenteral feedings the first 48 hours and were allowed milk and meat on the third day. At this time, unless technical errors resulted in early decline and death, the dogs were becoming increasingly vigorous (figure 19). The only indication of the procedure was diarrhea. However, about the sixth day abdominal distention often occurred, although the dogs continued to eat and were not obstructed. Despite the distention, the dogs were alert, eating, and up and about until only a few hours before death, which invariably occurred by the eighth day. During this time the typical pattern of white blood cell count, plasma hemoglobin, hematocrit and plasma volume was as shown in figure 20.

Autopsy findings in dogs with homografted bowel—Careful autopsy of dogs dying between the sixth and eighth days revealed few findings to explain their deaths. Clear ascitic fluid usually was present and had caused the distention. This may also have accounted for the gradually increasing plasma volume prior to death in that the "plasma space" had increased to include this peritoneal fluid because of an increased permeability of the vascular space as a result of immune responses between host and homograft. In all such dogs the bowel appeared viable (figure 21). This viability was confirmed on microscopic examination. Further, the microscopic sections did not show any extensive round-cell or plasma-cell infiltration or polymorphonuclear-cell infiltration so characteristic of rejected skin or kidney homografts (figure 22). This

TABLE 2

EXPERIMENTAL REMOVAL AND REPLACEMENT OF THE SMALL BOWEL

GROUP	NUMBER OF DOGS	MAXIMAL VALUES IN FOUR HOURS FOLLOWING REPLACEMENT OF BOWEL*		
		Plasma volume loss (per cent)	*Hematocrit increase (per cent)*	*Plasma hemoglobin increase (milligrams per cent)*
Bowel replaced in two hours	10	27.6 ± 14.8	20.1 ± 11.3	20.5 ± 27.9
Bowel replaced in five hours	10	35.4 ± 18	31.0 ± 7.1	17.9 ± 15

SURVIVAL WHEN BOWEL WAS REPLACED WITHIN TWO HOURS

Dog	*Survival*	*Cause of death*	*Condition of bowel at autopsy*
1	16 days	Multiple lung abscesses	Normal
2	7 days	Sacrificed	Normal
3	30 days	Sacrificed	Normal
4	12 days	Intussusception	Normal
5	4 days	Rupture of superior mesenteric arterial anastomosis	Ischemic necrosis
6	3 months	Sacrificed	Normal
7	6 months	Sacrificed	Normal
8	12 months	Sacrificed	Normal
9	18 months	Sacrificed	Normal
10	24 months	Sacrificed	Normal

SURVIVAL WHEN BOWEL WAS REPLACED WITHIN FIVE HOURS

11	7 days	Sacrificed	Normal
12	4 days	Leak of proximal bowel anastomosis	Normal
13	14 days	Sacrificed	Normal
14	30 days	Sacrificed	Normal
15	3 days	Pneumonia	Normal
16	5 days	Thrombosis of superior mesenteric vein	Hemorrhagic necrosis
17	3 months	Sacrificed	Normal
18	4 months	Sacrificed	Normal
19	12 months	Sacrificed	Normal
20	18 months	Sacrificed	Normal

*Mean values with standard deviations.

normal bowel confirmed the normal plasma hemoglobin found before death (see figure 20). Moreover, the anastomoses between the homograft and the host's duodenum and colon showed normal healing (figure 23). So we were faced with assigning a cause of death when the homografted bowel appeared normal; the other viscera also appeared to be normal, yet the dogs died by the eighth day.

It is entirely possible that the homograft of bowel elaborates substances at the time of rejection which cause a rapid metabolic death of the host before characteristic pathologic changes can develop—the so-called runt phenomenon in which the graft rejects the host.[16] In any event, although there is a dearth of the usual signs of rejection, the time of rejection agrees closely with that for kidney homografts and liver homografts in dogs.[17-19]

In contrast with the ease of measuring function of a homografted kidney, it is difficult to assess the degree of function of bowel transplants. However, digestion seemed to be at least reasonably effective, since undigested food was not found in the stool. Experiments are presently in progress to assess more ac-

TABLE 3

FATE OF SMALL BOWEL HOMOGRAFTS

SURVIVAL OF DOGS	NUMBER
0-2 days	7
3-5 days	4
6 days	4
7 days	7
8 days	2
Total dogs with homografts	24

curately the function of the bowel homografts and also to prolong the survival of these transplants as well as other transplants of stomach and spleen.

Other Visceral Grafts

Gastric autografts—Having had some success with transplants of the small bowel, our thoughts turned naturally toward other visceral organs which might lend themselves as autografts or homografts. Certainly from the surgeon's viewpoint there is no more important visceral organ than the stomach. Again, studying the anatomy of the dog's stomach which, like the bowel, is quite similar to that of man, we found that it was feasible to remove the stomach in such a manner that it could be revascularized by a single arterial and venous anastomosis.

The celiac axis of the dog is identical to that of man (figure 24), with the hepatic artery and splenic artery being of about equal size and the left gastric artery being the smallest of the three branches. The major blood supply of the stomach of the dog is from the left gastric artery and the short gastric branches of the splenic artery. The principal venous drainage of the stomach is by way of the left coronary vein and the splenic vein via the short gastric tributaries. Partial and complete occlusion studies of the blood supply of the stomach in vivo revealed that the stomach could withstand about the same degrees of ischemia as the bowel while still retaining viability when circulation was resumed. Again by trial and error, a method of removing the stomach for use as an autograft or homograft was developed.

FIGURE 19. Each of the dogs pictured has a homograft of the small bowel obtained from the other. Picture was made five days after operation. The dogs are drinking and eating.

Preparation of the stomach for transplantation—Adult mongrel dogs of either sex were used, and obviously the bigger the animal the better is the chance of getting good vascular anastomoses. The animals were anesthetized with sodium Pentothal and the procedure was carried out using aseptic technic. The pylorus was divided after division and ligation of the right gastric and right gastroepiploic arteries, followed by division of the lesser omentum. The distal half of the pancreas along the splenic artery and vein was resected in order to visualize the junction of the gastrosplenic trunk with the superior mesenteric vein. This area was completely cleared off so that the gastrosplenic trunk formed by the coronary vein and the splenic vein could later be divided flush with the superior mesenteric vein. The arterial and venous branches around the cardioesophageal junction were then divided preparatory to dividing the stomach from the esophagus. Usually about 2 cm. of stomach was left attached to the esophagus to facilitate the later replacement. The left gastric and splenic arteries were then freed of all nervous and connective tissue, care being taken to leave the hepatic artery untouched. In this respect, we often noted that following the dis-

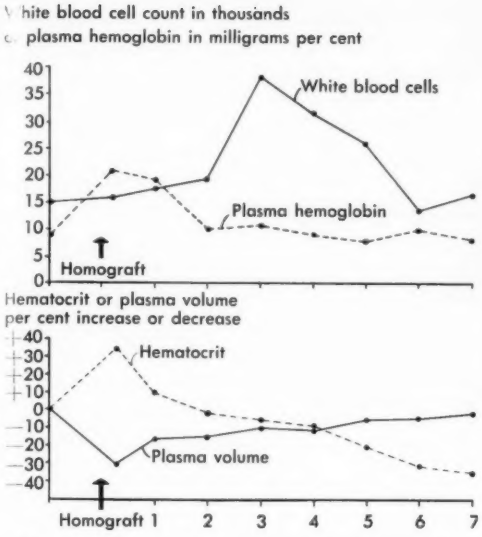

White blood cell count in thousands
Plasma hemoglobin in milligrams per cent
White blood cells
Plasma hemoglobin
Homograft
Hematocrit or plasma volume
per cent increase or decrease
Hematocrit
Plasma volume
Homograft 1 2 3 4 5 6 7
Time in days after placement of bowel homograft

FIGURE 20. Typical pattern of white blood cell count, plasma hemoglobin, hematocrit and plasma volume in a dog receiving a small bowel homograft. Note that although the dog died on the eighth day after placement of the graft, the plasma hemoglobin was normal at this time. This correlated with the normal appearance of the bowel at autopsy (see figure 21).

section around the celiac axis the liver darkened perceptibly, and this was often accompanied by a fall in blood pressure and subsequent failure of the animal to awaken from anesthesia when the surgery had been completed. The hepatic congestion usually could be avoided by giving a slow intravenous drip of the adrenergic blocking agent phenoxybenzamine (DIBENZYLINE®) in a dose of 0.25 mg. per kilogram during the period of dissec-

FIGURE 21. Small bowel homograft at autopsy seven days after placement. The bowel is normal in appearance.

FIGURE 22. Sections of small bowel autograft (*top*) and homograft (*bottom*). There is no microscopic evidence of rejection in the small bowel homograft even though this dog died in eight days.

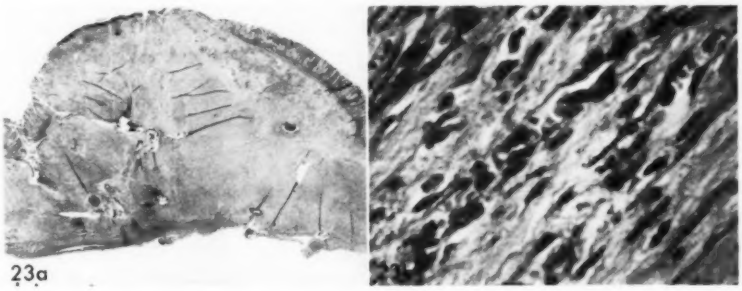


FIGURE 23. Low-power and high-power microscopic appearance of anastomosis between homograft of small bowel and host's bowel. Healing has proceeded normally with normal infiltration of the anastomosis with fibroblasts.

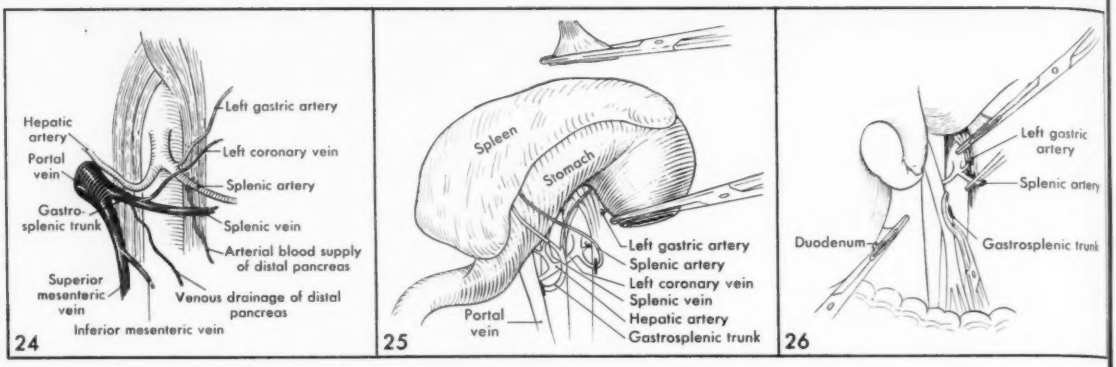


FIGURE 24. Anatomy of the celiac axis and the portal vein in the dog.

FIGURE 25. Removal of the stomach for use as an autograft or a homograft. The left gastric artery usually is divided and ligated unless its internal diameter is more than 2 mm. The stomach is then nourished by the short gastric branches of the splenic artery.

FIGURE 26. The stomach has been removed. Note that the gastrosplenic trunk has been divided almost flush with the portal vein.

tion around the celiac axis and hepatic artery.

The dissection of the celiac axis being completed, the stomach was pedicled on the gastrosplenic venous trunk and the left gastric and celiac arteries. If the left gastric artery was less than 2 mm. in diameter, it was divided, leaving the splenic artery to supply the stomach via the short gastric branches (figures 25 and 26). The spleen could be left attached to the stomach or removed, as long as the short gastric vessels were preserved. The procedure was completed by placing Kapp-Beck vascular clamps across the gastrosplenic vein at its junction with the superior mesenteric vein and across the splenic artery just distal to the hepatic artery, dividing these vessels, and removing the stomach (figure 27).

If the resected stomach was to be replaced

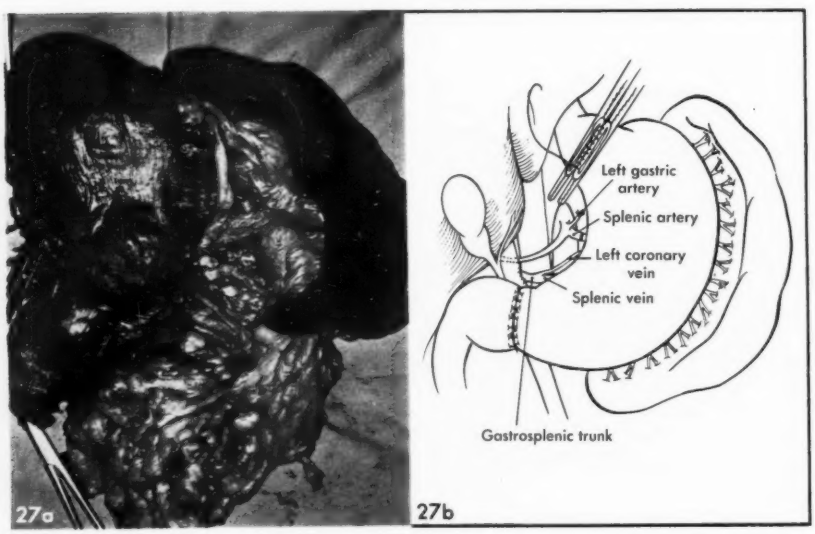


FIGURE 27. a. The resected stomach. The spleen can be left attached or removed and discarded as long as the short gastric vessels are preserved.

b. The stomach has been replaced as an autograft.

as an autograft or a homograft within two hours, no special effort to cool the organ was made other than allowing it to cool naturally to room temperature. If the stomach was to be held in vitro for a longer period, it was cooled quickly to 5° C. the way the bowel was cooled.

Again, when circulation was re-established the stomach regained its viability, with normal color and peristalsis. Circulation was restored by suturing the gastrosplenic trunk flush on the superior mesenteric vein. Both this anastomosis and the anastomosis of the splenic artery, and of the left gastric artery when feasible, were made with a running over-and-over 6-0 suture. The proximal end of the stomach was rejoined to the esophagus and tiny remnant of stomach with a two-layer open anastomosis. A similar anastomosis was used to join the distal end of the stomach to the duodenum. The abdominal cavity was then closed after a thorough rinse of the peritoneal cavity.

Results—The mortality rate for gastric autografts remains higher than the mortality rate for bowel autografts. The vessels are smaller than the superior mesenteric vessels, and in addition the end-to-side anastomosis of the gastrosplenic vein to the superior mesenteric vein is more prone to thrombose. However, we have obtained a number of long-term survivors, eight of which have now lived for periods ranging up to one year after autografting of the stomach. Figure 28 shows three of these dogs at varying periods following this procedure. These dogs are vigorous and appear normal in every way, with good appetites and normal stools. Plasma volume studies have again shown a loss of plasma as a result of the procedure which appears to be proportional to the length of time the stomach is held in vitro before being replaced. This deficit is restored rapidly as the animal recovers following surgery.

Functional studies of gastric autografts—What happens to gastric secretions in these dogs with autografted stomachs? What happens to gastric motility? Will the stomach empty? After all, the animals have had about as complete a vagotomy as is possible.

Figures 29 and 30 give examples of acid and pepsin secretion in these dogs at varying periods following the autograft procedure. In the fasting state these dogs had very low levels of pepsin and no free acid; the pH as a consequence was quite high. Now this is not unusual even for normal dogs, since dogs secrete acid and pepsin only in response to food, thereby apparently being better adjusted to the rigors of modern living than their masters. The surprising finding is that these dogs also do not secrete acid when given a triple histamine test (0.5 mg. histamine base given intramuscularly every 30 minutes for three doses), nor do they secrete pepsin when given the potent stimulation of pilocarpine (2 to 4 mg. intramuscularly). Repeated examinations up to six months later still show this fastness to histamine and pilocarpine, although after this period there is evidence of a gradual return of low levels of acid following histamine stimulation. Return of pepsin secretion appears to be delayed even longer. Perhaps this may be the operation of the future for ulcer. It certainly would please internists; how happy they would be if the surgeon always put back everything he took out. This procedure needs more study, and we are attempting to quantitate the duration and severity of ischemia required to destroy permanently most or all of the chief and parietal cells while still maintaining the viability of the stomach as a whole.

Gastric homografts—The number of these procedures is still small. The operation is carried out simultaneously on two animals, whose stomachs are transferred one to the other. It appears that gastric homografts, like bowel homografts, are tolerated about eight days before the new host dies. As with the bowel, few cellular signs of rejection of the stomach are seen microscopically, and anastomoses between the gastric homograft and the new host's esophagus and duodenum show a normal degree of healing.

Autografts of spleen—The experience gained in making small bowel and stomach transplants made the production of transplants of the spleen quite easy. Again the anatomy of the splenic circulation made it possible to remove the spleen and later replace it by

FIGURE 28. Three dogs which have had functioning autografts of the stomach for three, six and 12 months, respectively. They are normal in every way except that the ability of the stomach to secrete acid and pepsin seems to return only after a year or more following the procedure.

making a single arterial and venous anastomosis (figure 31). Ten such autotransplants of the spleen were made, and in only two of the dogs did the splenic vein thrombose and cause death early in the postoperative period. The other dogs were re-explored at periods of two weeks to six months following the procedure, and the spleen was seen to be viable. A further functional test of the circulation to and from the spleen was made by injecting 0.5 mg. of a 1:1000 dilution of epinephrine into the systemic venous circulation. In a few seconds the spleen contracted tightly as its contained blood was emptied into the systemic circulation, thus proving that both the splenic vein and the splenic artery were patent. The explored animals were then sacrificed and the splenic vessels were opened and inspected (figure 32).

Use of Splenic Autografts to Protect Against Irradiation

Autografts of the various visceral organs are of value because they show us much of the physiology of the organs under a new set of conditions, particularly under conditions where direct nervous connections are severed and any control must come from neural elements intrinsic to the organs or via the vascular system through hormones. In addition, experience gained in making the various autografts will obviously stand one in good stead for eventual construction of lasting homografts. This raises the question, what can be

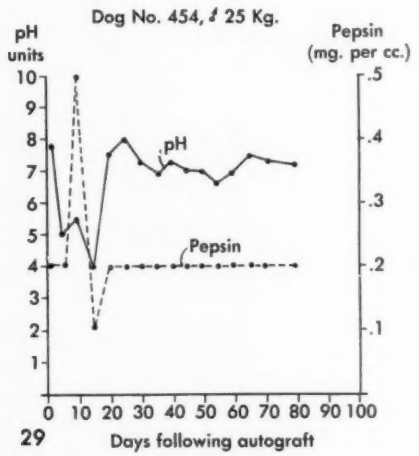


FIGURE 29. Acid and pepsin response to histamine and pilocarpine stimulation one month following gastric autograft. No free acid was found; pepsin response was negligible.

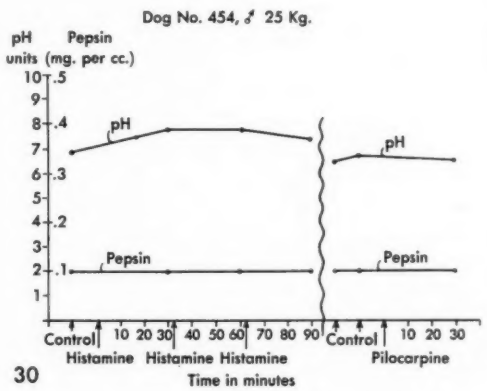


FIGURE 30. Acid and pepsin response to histamine and pilocarpine stimulation six months following gastric autograft. The results were the same as at one month, no free acid and negligible pepsin. One year following the procedure, pepsin secretion still was negligible after pilocarpine stimulation, but after histamine stimulation 25 degrees of free acid were measured.

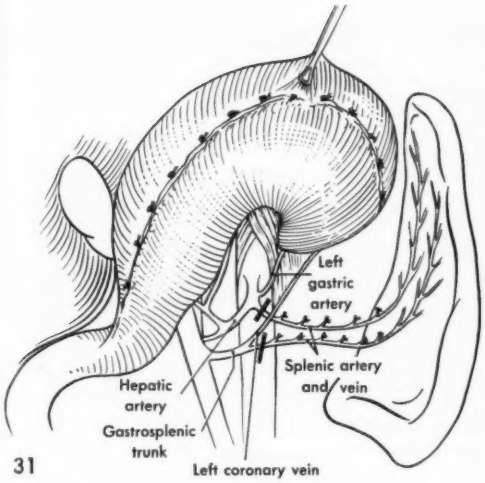


FIGURE 31. Technic for preparing autotransplants or homotransplants of the spleen.

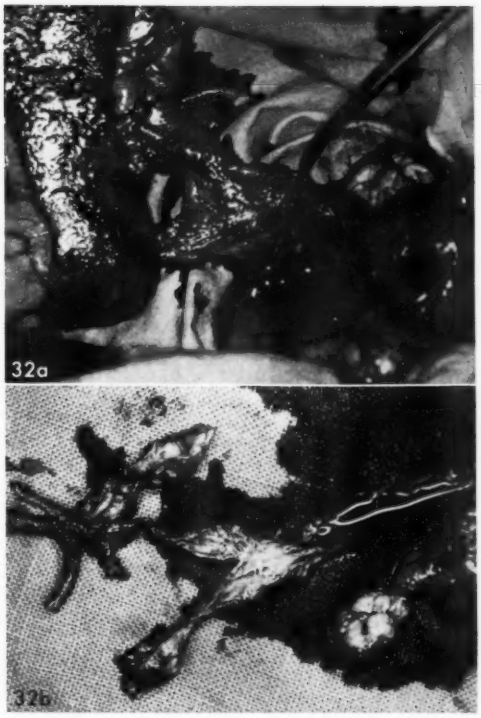


FIGURE 32. a. Autotransplant of spleen inspected six months following the procedure. The spleen contracted promptly following systemic intravenous injection of epinephrine, indicating patency of the splenic vessels.

b. The patent splenic artery and vein after sacrifice of the animal.

done to prolong the survival of homografts?

One way to prolong the survival of homografts is to weaken or ablate the immune responses of the new host with high doses of irradiation. The consequence of such a procedure is well known. This form of treatment destroys the blood-forming structure of the host as well as the immune responses, and precipitous death inevitably results from hemorrhage, infection and inanition. To protect the host against the lethal effects of irradiation while at the same time obtaining the desirable effect of the x-rays on the immune mechanisms causing rejection of foreign tissues was the goal of the experiments using splenic autografts.

Bone marrow has been shown to protect dogs against lethal body irradiation when used as an autograft or a homograft.[20] The spleen also is a rich source of similar cells needed to protect the irradiated animals from death due to infection. In mice, rats and guinea pigs, various splenic preparations are as effective as bone marrow in preventing lethal irradiation sickness.[21,22] Similar studies in dogs were not available. Therefore, in this study we evaluated three different preparations of spleen in the treatment of irradiation sickness.

Methods and procedures—Adult mongrel dogs of both sexes weighing 10 to 20 kg. were used in all experiments. The total body irradiation was delivered with a 250 KVP, 30 ma unit at a rate of 22.6 r per minute to anesthetized dogs which were laid on their sides and given half of the total exposure to each side. The doses given were "minimum tissue doses" calculated at the midsagittal plane of the dog. Prior to the experiment, bone marrow and blood samples were obtained for hematocrit and differential counts. These studies were repeated daily following the irradiation. Dogs were considered survivors only if they survived four weeks after irradiation. All surgical procedures were done using general anesthesia and aseptic technics.

Group 1 (controls)—Four dogs were given

TABLE 4

EXPERIMENTS IN USE OF SPLENIC AUTOGRAFTS TO PROTECT AGAINST IRRADIATION

GROUP	NUMBER OF DOGS	PROCEDURE	DOSAGE OF TOTAL BODY IRRADIATION	NUMBER OF SURVIVORS*
1	18	Controls	300 to 500 r	1
2	15	Autograft of intact spleen	500 r	1
3	11	Shielding of spleen	500 r	3
4	12	Autograft of homogenated spleen	500 r	10

*To be classed as a survivor, an animal had to survive four weeks or longer.

300 r, four received 400 r, and 10 received 500 r. Following irradiation, a careful check on nutrition was made and forced feedings and parenteral fluids were given as necessary. Antibiotics also were given daily.

Group 2—In 15 dogs, the spleen was removed *in toto* and stored in vitro at 5° C. while the dog was given 500 r. After irradiation the spleen was returned to the dog as an autograft by reanastomosing the splenic vessels to their proximal stumps, and the dog was followed as described for group 1. As noted, we had established previously that splenic autografting could be done in unirradiated dogs with indefinite survival of host and autograft.

Group 3—In 11 dogs the spleen was freed so that it could be placed in a lead box outside the abdominal cavity while still attached by the splenic vessels. These dogs also received 500 r. Following this, the spleen was returned to the abdominal cavity.

Group 4—In 12 dogs the spleen was removed and, while the dog was receiving 500 r, the spleen was sliced into pieces and passed through screens of successively finer dimensions.[23] The homogenate obtained was diluted with TIS-U-SOL® (Baxter Laboratories) and returned to the dogs as an intravenous autograft following completion of the irradiation. Homogenates so prepared contained from five to nine billion cells of which 90 to 95 per cent were viable when they were stained with neutral red.

Results—All but one of the 18 control animals were dead by the ninth postirradiation day (table 4). By the fourth day these dogs were anorectic and vomiting and required parenteral feedings. About the same time, white blood cells had begun to disappear from the peripheral blood, and near the time of death they usually numbered less than 100 per cubic millimeter. Almost all nucleated cells disappeared from the bone marrow during this same period. Dogs receiving an autograft of intact spleen (group 2) fared no better than the controls; only one of the 15 survived, and the rest died within nine days after irradiation. At autopsy these dogs were found to have hemorrhagic pneumonia, as did the control animals. In almost all instances the anastomoses of the splenic vessels were patent and the spleen had been viable prior to death. Splenic shielding (group 3) perhaps conferred a low level of protection, since three of 11 dogs in this group survived. However, the results in the dogs receiving an autograft of homogenated spleen (group 4) were striking compared with the outcome in the first three groups. Ten of 12 dogs in this group survived, and these dogs followed a clinical course distinctly different from the others. Although the white blood cell count dropped as low as 300 per cubic millimeter (figure 33), these dogs did not become anorectic, did not vomit, and did not require parenteral feedings. Selected survivors sacrificed at varying periods after four weeks showed only atrophic gastrointestinal mucosa and hypertrophied mesenteric lymph nodes. No late deaths have occurred in this group, which has been observed for periods up to nine months.

It is evident from these data that the homogenization of the spleen releases or makes

available substances or cells which are not available from the intact spleen whether autografted as a whole organ or shielded. Furthermore, the splenic homogenate is as effective as bone marrow in our hands in preventing death from lethal irradiation and should be considered along with bone marrow in any regimen used to treat acute irradiation sickness resulting from attempts to alter immune responses with x-rays.

Bone-Marrow Transplants

Brief mention should be made of other methods used in this laboratory to protect dogs against the lethal effects of irradiation while still retaining the beneficial effect of the irradiation on the immune responses of the dog. Both autologous and homologous bone marrow have been used to prevent the death of dogs given supralethal doses of irradiation. The autologous bone marrow has been removed from the dog prior to the irradiation and then returned as an intravenous infusion following the irradiation. With this method it has been possible to protect dogs against doses of irradiation ranging as high as 1000 r so far. Obviously the desired end result is to be able to give a homograft of homogenized spleen or bone marrow from a donor to a new host which has been irradiated. If this infused blood-forming tissue can establish itself in the bone marrow and reticuloendothelial system of the new host, it will then be possible to achieve prolonged survival of organ homografts, such as described herein, from the same donor which supplied the spleen or bone marrow initially. These studies are in their infancy, but it is immediately apparent that supralethal doses of irradiation in the range of at least 1200 to 1500 r will be required for even temporary success in this field, for both in dog and in man the dose of irradiation required for such an effect is four to five times the lethal dose of total body irradiation.[24]

Conclusion

In closing, I would like to recall one of the earliest recorded medical meetings which was described by the medical historian Felix Marti-Ibañez.[25] It was held more than 2000 years ago at the house of Agathon in Athens, "by the light of torches that sparked the wine goblets into a myriad of rubies. Eryximachus, the physician, defined medicine to the other guests, among whom was Socrates, as the study of the love affairs of the organs of the body." I doubt whether a better definition could be given today. Certainly this definition also applies to the transplantation field. We have the new host and the homograft living temporarily in perfect harmony, as is true of many a contemporary connubial union, only to have the brief idyllic interlude interrupted by abrupt rejection, one of the other.

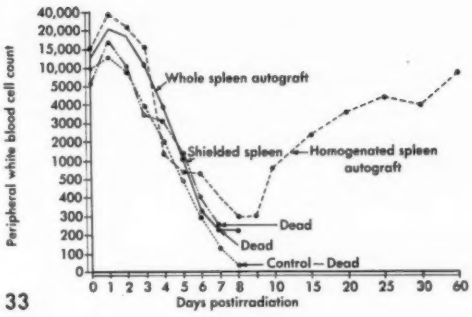


FIGURE 33. Response of peripheral white blood cell count in typical total body irradiation experiments (500 r).

The experiments described herein are merely abrasions on the surface of the manifold problems to be solved before this "love affair" between host and homograft can be made lasting. Yet the portent for the future of this and similar experiments presently being carried out all over the scientific world is obvious. Worn-out or diseased organs will some day be replaced at will, and new years engrafted on a life span already doubled in the past century. Are we ready for this horizontal extension of life, or will this be another example, as with the atom, where science may be outstripping sociology? It is to be hoped that equal vigor will be exerted in the years ahead to enrich and renew the soul as well as the substance of man.

The exciting prospects for surgeons in this field recall the words of Shakespeare's Brutus: "O that a man might know the end of this day's business ere it come."

ACKNOWLEDGMENTS

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Part 2 of this group of papers on Emergency Surgery for General Physicians will appear in the April issue.

Diagnostic Approach to the Infant With an Enlarging Head

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DEFINITIVE diagnosis of mechanisms of abnormal enlargement of the head in infancy is determined by the following steps:

Step 1. Routine radiographic examination of the skull.

Step 2. Investigation of the subdural space.

Step 3. Investigation of the ventricular system.

a. Ventriculography.

b. Pneumoencephalography.

Candling, electroencephalography, dye elimination studies and hydrodynamic studies without air do not provide definitive information relative to the mechanisms of head enlargement.

Adapted from an exhibit shown at the annual meeting of the American Medical Association, Atlantic City.

Step 1

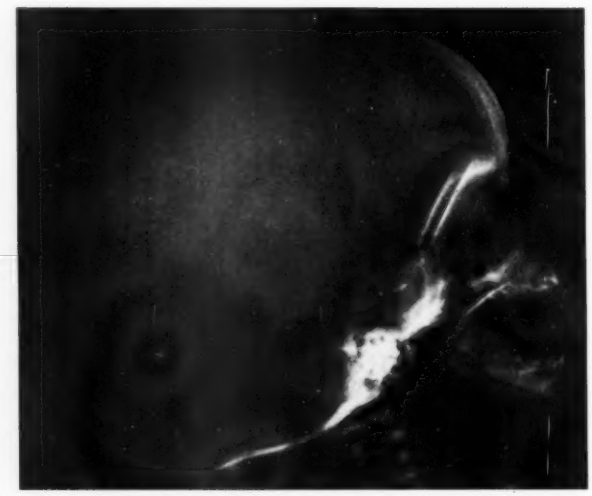
Routine Radiographic Examination

A. Internal hydrocephalus

1. Split sutures.
2. Thin bones.
3. Small posterior fossa.
4. Vault large compared with facial bones.

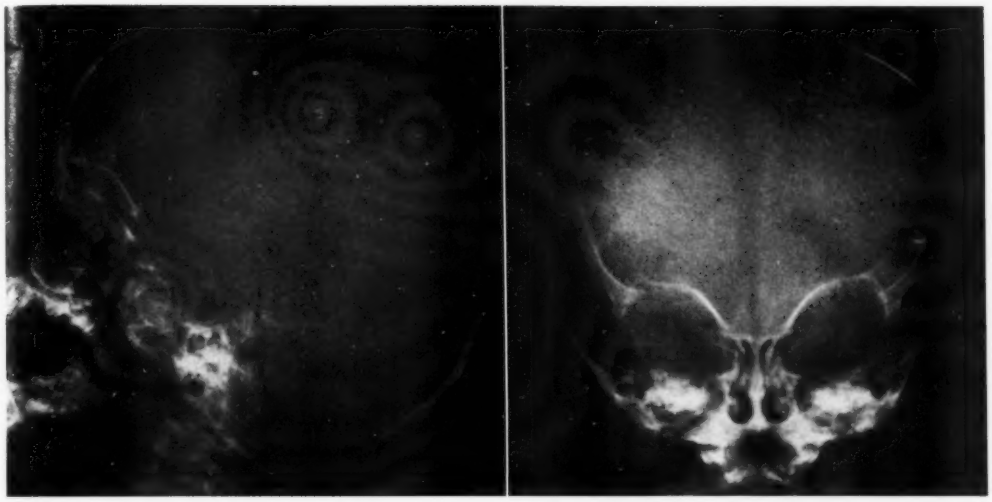
B. Communicating hydrocephalus

1. Vault large compared with facial bones.
2. Splitting of sutures not as marked as in A.
3. Bones may not be thin.



C. Cyst of the fourth ventricle

1. Elongation of the posterior fossa.
2. Normal anterior fossa.



D. Tumor of the posterior fossa

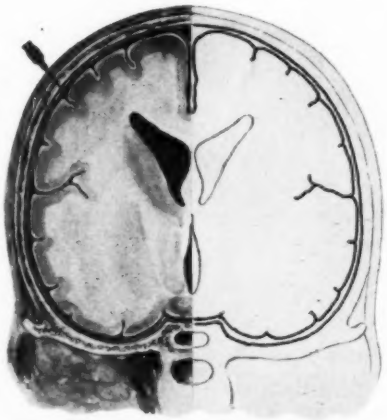
1. Split suture lines.
2. Thinning and often bulging of the posterior fossa.

E. Tumor of the hemisphere

1. Asymmetric enlargement.
2. Thinning of the bone over the lesion.
3. Intracranial calcification may be present.

Step 2

Subdural Tap



← Positive Negative →

If tap is negative, step 3:
Increased intracranial pressure—ventriculogram.
Normal intracranial pressure—pneumoencephalogram.

Subdural Collections

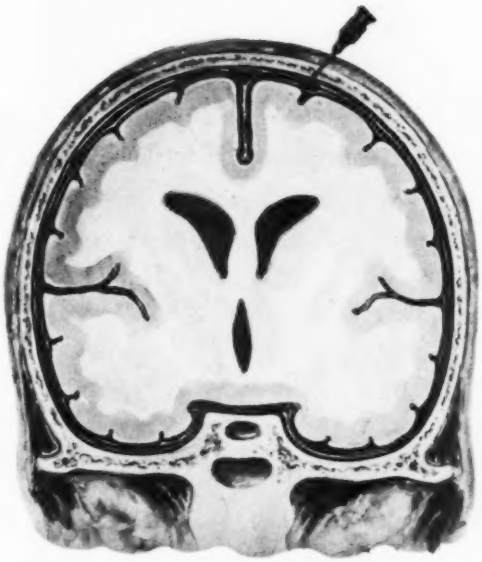
Air in subdural space.

Acute subdural hematoma. *Top:* Symmetric vault and split sutures. *Bottom:* Subdural tap yields dark, sanguineous fluid.

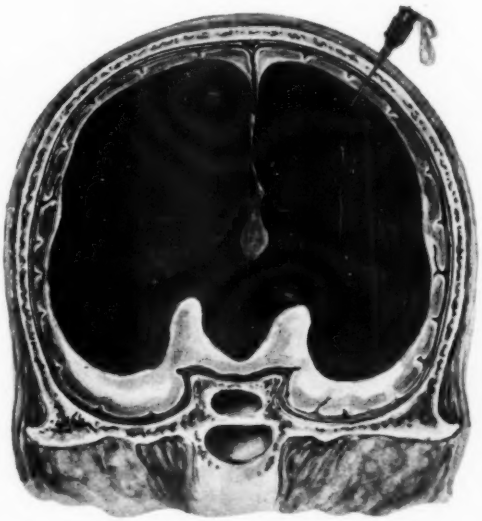
Chronic subdural collections. *Top:* Biparietal prominence of vault. *Bottom:* Tap yields thin xanthochromic fluid with elevated protein content.

False Positive Findings on Subdural Tap

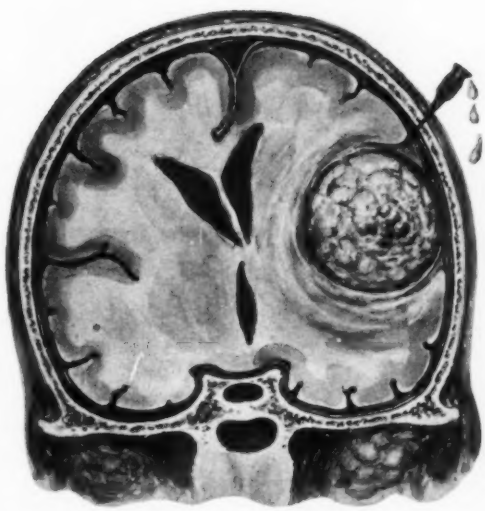
Tap into subarachnoid space. Clear, colorless fluid with low protein content.



Tap into cortical vein yields venous blood.



Tap through cortex into widely dilated ventricle may be interpreted as subdural collection. Fluid is usually clear and colorless with a low protein content.

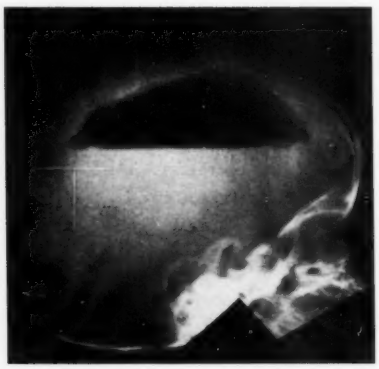


Tap into dilated subarachnoid cyst over tumor may simulate chronic subdural collection by producing xanthochromic fluid.

Step 3

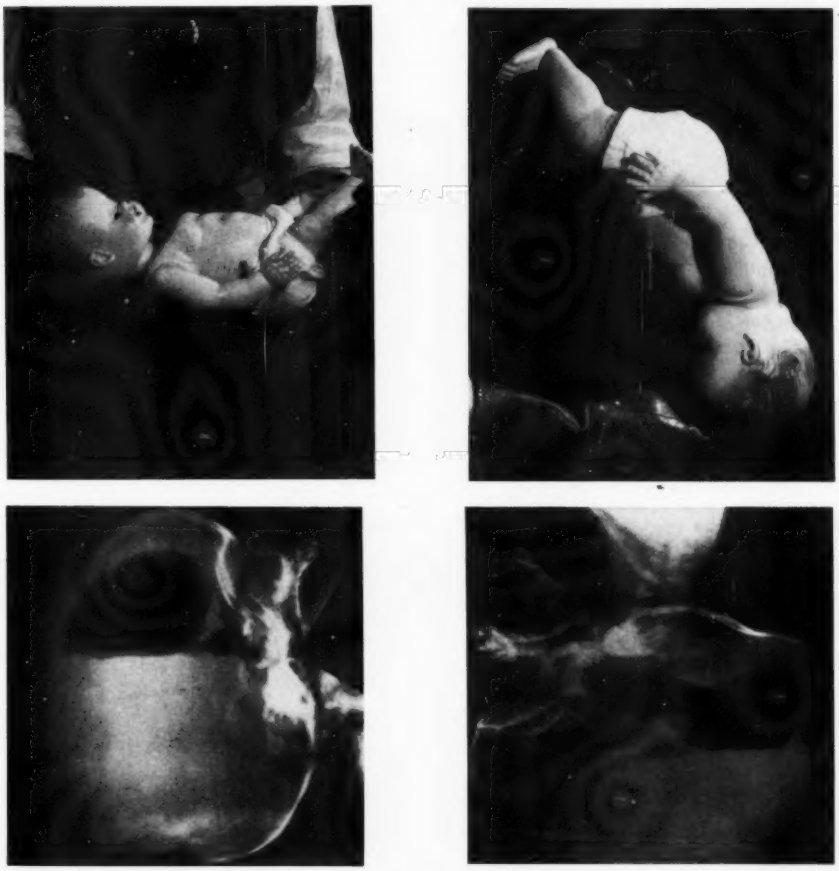
Ventriculography

Needle puncture through coronal suture line into ventricle of nondominant hemisphere with exchange of not more than 40 to 50 cc. of air.

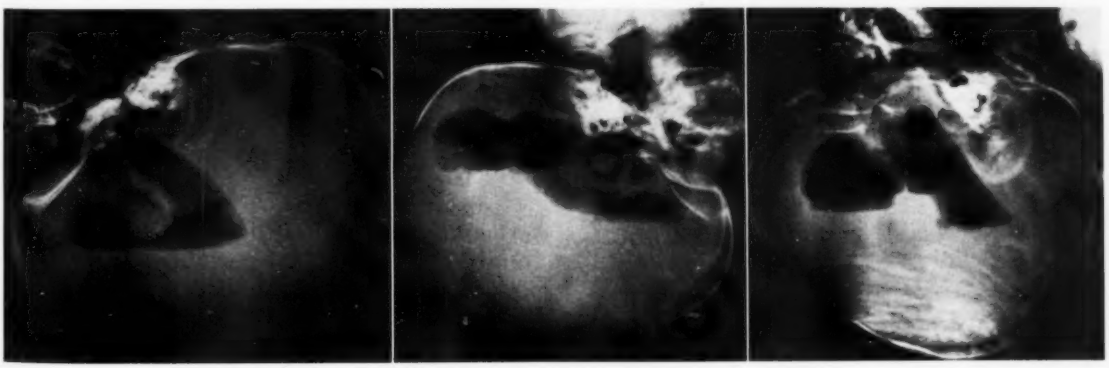


Maneuver for displacing air from lateral ventricle into third and fourth ventricles.

Maneuver for displacing air from lateral ventricle into third and fourth ventricles.



Air displaced into fourth ventricle and spinal canal demonstrating communicating hydrocephalus.



Cyst of fourth ventricle. Anterior displacement of ventricular system.

Stenosis of aqueduct. Blunt and in normal position.

Tumor in posterior fossa. Aqueduct displaced anteriorly and pointed by extrinsic pressure.

Pneumoencephalography

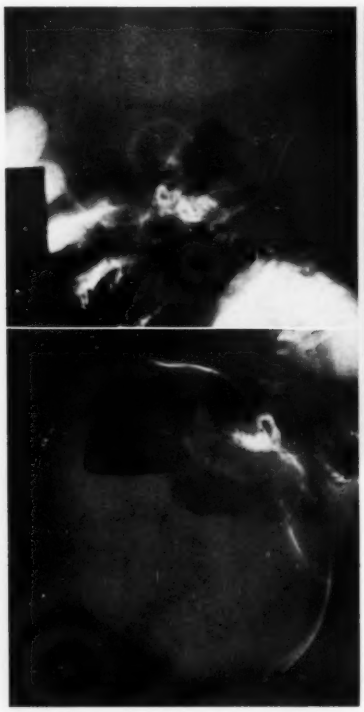
Pneumoencephalography, the more precise study, provides visualization of basilar cisterns and subarachnoid pathways.

1. As primary study in absence of increased intracranial pressure.
2. As adjunct to ventriculography for better visualization of the posterior fossa.

Method: Air is injected before fluid is removed (positive pressure technic of Lindgren and Robertson).

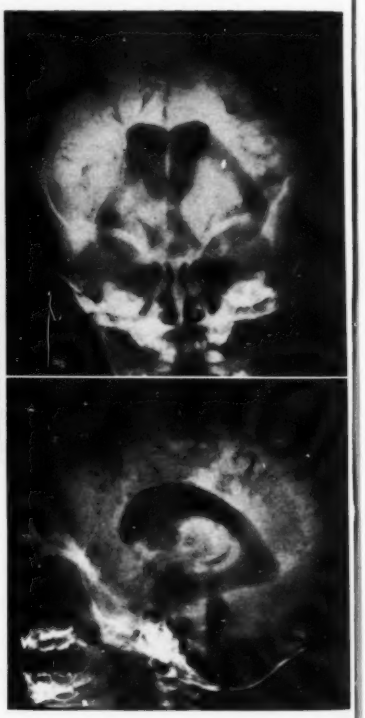
Position of head for selectively filling ventricular system.

Position of head for selectively filling basilar cisterns.



Arachnoiditis of posterior fossa with partial block. Ventriculogram *(bottom)* demonstrates partial block in posterior fossa. Pneumoencephalogram *(top)* demonstrates pocketing of air in posterior fossa.

Tumor of left hemisphere. Shift of ventricular system to right.



Subdural hematoma previously demonstrated by subdural tap. Pneumoencephalography performed to eliminate additional abnormality.

PSYCHOSOMATIC MEDICINE—*Fifth of a Series*

Differentiation of Neurosis From Organic Disease

JOSEPH FRANKLIN GRIGGS*

The Claremont Medical Research Foundation, Inc., Claremont, California

Introductory Comment

It is a sign of the times, perhaps even a badge of maturity for modern medical practice, that the spotlight falls increasingly on the concept of "whole-person" diagnosis and treatment of illness. For we educators who have grown scarred and weary in the wars of preaching this to young medical students, the trend is encouraging and rewarding. The concept, and full orientation to it, is only a first step, however. Much remains to be done in developing anchoring definitions for the organic-neurotic continuum, in developing and testing diagnostic criteria, and, of course, in correlating treatment methods with diagnoses. By sharing his own personal "scale of norms," developed over the course of many years, Dr. Griggs has offered an approach and a challenge to this monumental task. It remains for many others to contribute their time, thought and experience in the arduous task of refining our use of the organic-neurotic continuum. It means that we must sharpen ourselves as instruments of medical insight, that we must objectify our clinical fantasy, that we must "come of age" in the use of the chemical and mechanical tools provided to us by what we might term the "purer" sciences. The reading of this article is only for those who would be disquieted and provoked to meditate upon the imponderables.—Franklin G. Ebaugh, M.D.†

NEUROTIC states are so common that physicians in general practice are taught to expect that 60 to 80 per cent of their patients will require no treatment for organic disease. Postgraduate courses in which general practitioners are taught by psychiatrists to support and listen to these neurotic patients are increasingly offered throughout the United States. The psychiatrists, more than busy enough already, are happy to leave the "neurotics" in the general physician's hands and to teach him how to keep them there. One of our venerated teachers has taught us to recognize a neurosis "in a moment,"[1] but the student gets the impression that once this is done the search for any organic disease is a waste of time and money.

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When our fathers and grandfathers practiced medicine the idea that wrong thinking caused disease was a heresy, like Christian Science which is no science at all.[2] But the psychogenic concept has won such a place in our thought today that actual organic disease too often goes undetected. It is easy to detect emotional maladjustments or traumatic early histories or unloved feelings in almost any patient. An initial diagnostic impression of neurosis, like an early impression of a serious organic disease, requires some positive proof in terms of clear criteria. Such confirmation cannot be established in a few minutes.

JOSEPH FRANKLIN GRIGGS

It has been a sound rule to expect each patient to have only one basic organic disease at a time, and it certainly simplifies teaching. But the rule leads to too much oversimplification when it is extended to the differential diagnosis of organic *versus* "functional" illness. It is more realistic and comprehensive to ask, "How much of this patient's illness is emotogenic and how much is organic defect or disease or deficiency?" It is an error of oversimplification to assume that the discovery of either one, an organic disease or an emotogenic illness, excludes the other.

Clinical Experience

After a quarter of a century it seemed pertinent to review my experience in the practical task of differentiating neurosis and organic disease in the general practice of medicine and surgery. In classification the patients fell into the following categories: (1) neurosis with little or no organic disease, (2) psychosomatic or "stress" disease with organic or allergic changes, (3) organic disease with little or no neurosis superimposed, (4) neurosis combined with organic disease, and (5) nonsymptomatic periodic examinations.

On review of these cases, there were fewer patients with pure neurosis than expected and more cases of neurosis combined with chronic organic disease. In many of these cases it appeared that there might not have been any neurosis if the organic disease had not been present as an inciting factor.

Our problem is to differentiate the first and second categories (emotogenic) from the third and fourth (organic) and from each other, as well as to assess the respective roles of neurosis and organic disease in the second and fourth categories.

Definitions

The most useful way to define our terms is to state the diagnostic features of each of the conditions to be differentiated. If these definitions are operational the differential criteria can be derived readily.

Definition of Neurosis

For a physician's purposes, neurosis must be defined in relation to complaints of illness and disability for which the patient consults a doctor of medicine. This is the manifestation of neurosis which concerns the physician. Thus it is more nearly synonymous with hysteria, "hypochondriasis" or "neurasthenia" in the older terminology than with the broader psychiatric definition of neurosis as "any disorder of the psyche."[3] To the medical practitioner a "neurotic" is a patient who is presenting complaints which suggest possible somatic illness, especially to the patient, when the only discoverable reality by the doctor is emotional or mental ill health. This definition implies that a physician does not diagnose a condition as a neurosis until he has ruled out organic diseases suggested by the symptoms, has *identified* a neurotic state, and can show how it is competent to explain the total clinical picture.

A snap diagnosis of neurosis not only is resented by the patient but is a reflection on the physician. It is also therapeutically disadvantageous because even if the physician's initial impression is correct and neurosis is the only illness present, the patient will not be convinced that organic disease has been ruled out or that mental illness has been proved. Any confidence or rapport which may

le established under these circumstances is only spellbinding and will not last through any adequate period of therapy, either with that physician or with his psychiatric consultant. However, there is the patient who comes with the hope that his symptoms can be dismissed quickly on the grounds of a temporary emotional disturbance of which he is aware. This is typically a person who is habitually on the job, not given to quitting easily for minor reasons. He is checking up on some symptoms because he has been told it is good preventive medicine to do so. He doubts that he is really sick. He is not truly neurotic. In this patient there is an important place for an expeditious diagnosis of emotogenic symptoms and reassurance that they will pass. Even here the physician has the responsibility to rule out organic disease by definite criteria. More often it is the chronically ailing and recurrently ill person who presents the real problem to the physician in the differential diagnosis of neurosis *versus* organic disease.

Differential Criteria of Neurosis

1. Neurosis must be included in the diagnosis whenever the patient uses any aspects of the illness to escape from or to excuse himself from his appropriate responsibilities, opportunities or relationships. This mechanism is an unconscious device which usually deceives the patient himself. Thus it is in sharp contrast to the malingerer's conscious intent to deceive others than himself. The neurotic is the first to be deceived about himself and the last to believe what he is doing. Disabled neurotics who are unable to perform certain duties are often efficient and conscientious about other obligations which do suit them, for example, entertaining or keeping up a large correspondence or advising their grown-up children.

2. Neurosis may be included in the diagnosis if the patient uses the illness to obtain other satisfactions extraneous to the disease and its symptomatology. This includes using unnecessary doctor's visits to substitute for social life, friendship, love, etc., to impoverish a hated husband or to obtain sympathy, to attain fashionable status, to lean on a father figure, or to "adopt" a bright young man—the physician.

3. Neurosis may be included in the diagnosis if the patient repeatedly sabotages effective treatment. When an ailment is somehow precious to the patient he finds some reason to change doctors or to stop treatment at the point when he sees that therapy is about to require him to behave or perform like a healthy person.

4. Neurosis may be included in the diagnosis if the patient displays an intractable disability due to fears or lack of stamina so deep-seated in the personality that hope of cure has been abandoned by all concerned. This condition is probably better included among the psychoneuroses. It has also been referred to as psychasthenia and constitutional inadequacy.

5. Neurosis is not justified as the medical diagnosis when the aforementioned criteria are not satisfied, nor is it justified simply because the physician cannot diagnose an organic disease, or because the patient gives an unsystematic and dramatic history with bizarre symptoms, or because of numerous surgical operations and multitudinous diagnoses in the past, or any similar superficial suspicion of a neurotic state. *Where the illness is providing no escape from life and work, it is not a neurosis.* Patients with organic illnesses and persons with certain psychoses can keep working to the edge of exhaustion for years, but the neurotic patient is the one who has the "exhaustion" and the illness in order to avoid, unconsciously, the work or other responsibility.

6. Even when a neurotic reaction pattern is identifiable, a diagnosis of neurosis is not sufficient if it is not competent to explain the entire clinical picture. When a patient fails to recover from a somatic disease within the usual prognosticated period of time one should consider whether the disability is being prolonged by the patient's discovery of some neurotic satisfaction in it. But when the past history of such a patient shows singular freedom from neurotic behavior prior to the attack, one should suspect a persistence of the organic disease rather than a basic neurosis, or

in addition to a reactive neurosis. Hundreds of patients in my experience have been rehabilitated by new therapeutic attacks[4,5] on old ailments which other doctors considered cured long ago. Many of these patients were thought by family and friends to be merely neurotic and "frail" or were diagnosed "postinfectious neurasthenia" by their doctors for so long a time that they came almost to believe it themselves and to behave neurotically to some extent, with appropriate guilt feelings, resentment, or both. The clue to these patients was that they were really doing their best to carry on, not to escape their duties. They had chronic disease or sequelae of some illness whose termination is not demonstrable objectively and which is merely assumed to be "self-limited." These are cases of iatrogenic neurotic reaction superimposed on an unrecognized persistent somatic disturbance.

By making an unwarranted diagnosis of organic disease on mere suspicion, iatrogenic neurotic reactions can also be superimposed on a patient who has simple anxiety without organic disease. This can be a serious disservice to a patient who is already basically neurotic, because it confirms him in his delusion of disability. However, in persons who are not basically neurotic this reaction is temporary and easily dispelled. In contrast, a really neurotic patient is not cured by the physician's authoritative reassurance that there is no organic disease present, and neither is the patient whose organic disease has been missed.

The physician should require his diagnostic study to answer the following questions about a presumed neurosis.

From what is the patient escaping by means of this illness?

Would she really prefer to be well? (Neurosis seems to occur 10 times more frequently in women than in men.)

Does she meet her obligations in spite of her symptoms or does she surrender to or hide behind her illness?

Is her illness her only means of escape?

When she really needs to escape, as anyone needs a vacation occasionally, does she often succeed in effecting it without resort to neurotic illness?

Does she need to be as sick as *this* to escape from *that*?

Is my diagnosis of neurosis well founded on criteria or is it only a suspicion or an impatient wishful thinking?

Am I dodging a difficult job of diagnosis and treatment by hiding behind the patient's presumed neurosis?

Is my diagnosis of neurosis sufficient to explain all features of the patient's illness?

Is my diagnosis of neurosis adequate to lead to helpful therapy?

Psychosomatic or Stress Disease

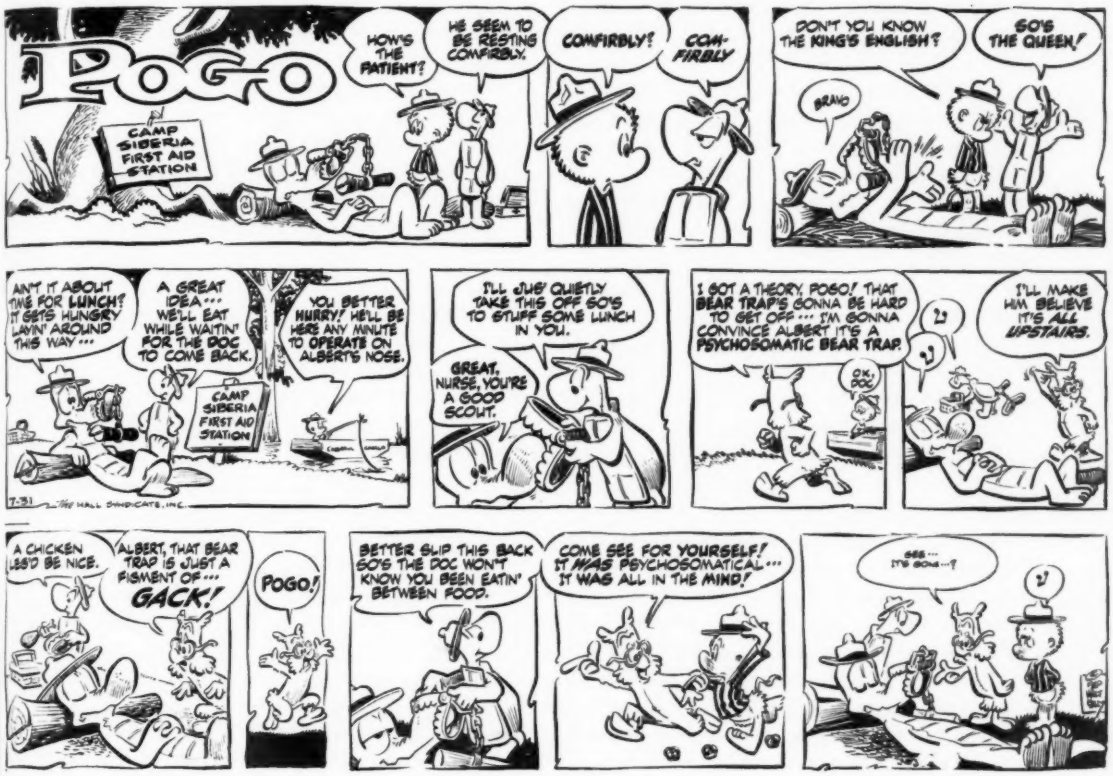
In this category the role of emotional reactions to external and internal stress is assumed to be primary and causal, but there are physical and physiologic consequences which, in time, result in organic disease. Classic examples are peptic ulcer, ulcerative colitis, asthma and other allergic manifestations, dermatoses, probably exophthalmic goiter to a certain extent, and some forms of hypertension and hypoglycemia; even atherosclerosis may be accelerated perhaps by psychosomatic hypercholesteremia.

It is well known that comparable degrees of stress and emotional tension bring a psychosomatic disease to some persons and none at all to others. Therefore, another important factor lies in constitutional proclivities which determine the onset, location and nature of resulting changes in tissues and functions.[6,7]

Differential Criteria of Psychosomatic Disease

1. Psychosomatic disease must be included in the diagnosis if there is found a disorder of tissues or function preceded by a period of unrelieved stress when the disordered changes are characteristic of known effects of such stress. A cause-and-effect sequence should be traceable, usually operating through the hypothalamic, autonomic nervous and endocrine centers to appear in target tissues and organs as somatic diseases. Hereditary predispositions to such diseases are well known to students of human constitutional medicine.[8]

2. Psychosomatic disease may be included in the diagnosis if the illness is complicated


POGO
CAMP SIBERIA FIRST AID STATION
HOW'S THE PATIENT?
HE SEEM TO BE RESTING COMFIRBLY.
COMFIRBLY?
COM-FIRBLY
DON'T YOU KNOW THE KING'S ENGLISH?
SO'S THE QUEEN!
BRAVO
AIN'T IT ABOUT TIME FOR LUNCH? IT GETS HUNGRY LAYIN' AROUND THIS WAY...
A GREAT IDEA... WE'LL EAT WHILE WAITIN' FOR THE DOC TO COME BACK.
CAMP SIBERIA FIRST AID STATION
YOU BETTER HURRY! HE'LL BE HERE ANY MINUTE TO OPERATE ON ALBERT'S NOSE.
I'LL JUS' QUIETLY TAKE THIS OFF SO'S TO STUFF SOME LUNCH IN YOU.
GREAT, NURSE, YOU'RE A GOOD SCOUT.
I GOT A THEORY, POGO! THAT BEAR TRAP'S GONNA BE HARD TO GET OFF... I'M GONNA CONVINCE ALBERT IT'S A PSYCHOSOMATIC BEAR TRAP.
OK, OK!
I'LL MAKE HIM BELIEVE IT'S ALL UPSTAIRS.
7-31
THE HALL SYNDICATE, INC.
A CHICKEN LEG'D BE NICE.
ALBERT, THAT BEAR TRAP IS JUST A FISMENT OF... GACK!
POGO!
BETTER SLIP THIS BACK SO'S THE DOC WON'T KNOW YOU BEEN EATIN' BETWEEN FOOD.
COME SEE FOR YOURSELF! IT WAS PSYCHOSOMATICAL... IT WAS ALL IN THE MIND!
SEE... IT'S GONE...?

Copyright, 1960, Walt Kelly

by autosuggestion on the part of the patient or through the influence of his family or friends. This usually is the result of fears and prejudices against the medications or other forms of treatment for their possible side effects or toxicity. This kind of suggestion can be so strong as to cause intolerance, somatic changes, hypersensitive overreactions and additional illness which may be quite unpharmacologic.

3. Psychosomatic disease may be included in the diagnosis when the organic disease is known to be practically always emotogenic in part of its etiology. Examples are asthma in childhood, where the emotogenic factor may vary from 10 to 90 per cent of the etiology,[9] and ulcerative colitis, according to some authorities.[10] However, the partial nature of the psychosomatic aspect must be respected and other factors sought.

4. Psychosomatic disease is not justified as the diagnosis when the organic change cannot be causally connected with a preceding period of unusual stress. Peptic ulcers, for example, often are more closely correlated to the seasons of spring and fall than to fluctuations in stress. When chronic stress is well borne, the sudden appearance of a disease should suggest one or more additional etiologic factors or a constitutional breaking

point. Herpes zoster, for example, may be preceded by stresses which seem causal, but it also appears "out of the blue" or after exposure to varicelloid viruses.

5. Psychosomatic disease is not justified as the diagnosis when a stress situation produces no somatic deviations from normal. A person who is complaining of ease of fatigue or difficulty in mental concentration because of a recognized stressful circumstance in his life is reacting to the stress but not with the production of an abnormal state or disease. He is having a normal reaction. The point at which insomnia and fatigue produce abnormality is not a definite one, and unless somatic changes appear, the differentiation does not lend itself to dogmatic criteria.

6. An important differential point between psychosomatic disease and neurosis is that the victim of psychosomatic disease accepts and endures stress until some tissue or function fails, whereas the neurotic avoids the stress and excuses herself from it by retreat into an adopted illness which saves her from both the stress and the organic sequela to it. Hers is a self-adopted stress from which she suffers, but not too much. There is some satisfaction in this kind of suffering. A diagnosis of neurosis should not be made until this mechanism is clearly identified and found to be a paying proposition from the patient's standpoint.

Organic Disease

1. Organic disease is present whenever morbid tissue changes have occurred to an extent sufficient to cause symptoms or malfunctions; or when deficiencies and excesses have disturbed the physiologic balances and rhythms of the body processes; or when allergic developments complicate the body's protective responses to diseases and treatments for them.

2. Organic disease cannot be excluded when there is a verified objective sign of alteration of good health beyond the ranges of normal—for example, fever; physical findings, including repeatedly elicited tenderness, even though unexplained by objective signs; increased sedimentation rate of erythrocytes; and other laboratory criteria, including any evidence of hyperallergic reactions.

3. Organic disease should be suspected whenever the patient has had a chronic infectious granulomatous disease or a collagenous or neoplastic or other organic disease known to show a proclivity for chronicity, recurrence or deteriorative effects. Location of previous disease also requires consideration. A patient who has had any abdominal surgery or peritoneal disease is liable to constricting, obstructing adhesive bands at any subsequent time, and his vague abdominal pain should not be passed off as neurotic or psychosomatic even if he complains in a typically neurotic style. Late sequelae of the chronic infections were better appreciated a generation ago than they are in the present era of antibiotics and psychosomatics.

4. Organic disease cannot be ruled out by finding a neurotic pattern in the patient.

5. Organic disease should be searched for seriously in a "neurotic" patient who persists in trying to meet life responsibly, or who has had psychotherapy with little or no success but continues to seek aid from the medical profession, or who demonstrates a willingness to give up the symptomatic crutches such as sedatives, stimulants, analgesics, tranquilizers, soporifics, and habits of overdependence and escape. One should remember how many blameless persons in the South were considered to be "shiftless no-accounts" before hookworm disease and nutritional deficiencies were recognized less than 60 years ago.[11]

Neurosis Coexisting With Organic Disease

That neurosis and somatic disease do coexist in the same patient is a common observation in the practice of medicine as well as a logical deduction from the foregoing differential criteria. It is a reflection of four facts:

1. The many satisfactions obtainable through neurotic behavior make it a very common condition in its minor forms. Therefore, in any group of organically ill persons a considerable number must be expected to show some neurosis.

2. Confirmed neurotic persons can and do get organic diseases in spite of taking such

good care of themselves. One remembers the epitaph of the deceased neurotic patient: "I kept telling you I was really sick."

3. When any portion of the total person is sick, as in either neurosis, psychosomatic disease or organic disease, the other portions of the person also become susceptible to suboptimal function. The concept of the unity of the total organism precludes sharp demarcations of soma and psyche. Thus an organic disease, especially a prolonged one, can ignite the tinder of a latent neurotic wish to be excused from impending responsibilities. Similarly a neurosis alone may eventually make impossible the vigorous normal healthy responses of the body.

4. Convalescence from either a neurosis or an organic disease is commonly prolonged by the concurrence of the other. Psychotherapists would be wise to refer their refractory patients to medical consultants for re-evaluation of the total diagnosis.

After the objective signs of a disease have disappeared and the patient remains ill, has she become neurotic?

What is expected of her when she gets well? Challenges? Opportunities? Or "burdens"?

If she is not unconsciously avoiding recovery through neurosis, does the physician have the humility to doubt the reliability of his therapy to bring about a complete cure of the somatic disease?

Can he doubt the "tests" that are supposed to indicate that she has recovered?

Does he remember that syphilis, for example, was thought to be a self-limited disease for centuries?

Does he remember that for many decades persons with low back injuries and persistent sciatica were considered malingerers and neurotics seeking compensation, until the discovery of herniated disk disease in our own lifetime?

Does he think of the probability that even our own teachers of today perpetuate some errors which will be uncovered tomorrow?

Therapeutic Tests

There are cases in which no differential diagnostic study will enable the physician to rule out completely either neurosis or organic disease. Shall we treat the suspected, but unproved, organic disease(s) or the probable neurosis? Or shall we pass the patient along to still another diagnostic center? It is my practice to put the problem clearly to the patient. He may elect to take treatment for a possibly persisting disease, or he may elect psychotherapy with a psychiatrist. He may not get well until both are done. He may choose to do both at once. For his own sake I advise the latter, but because of my own curiosity I hope he does only one at a time so that we can have something in the nature of a therapeutic test of his diagnosis.

The criticism of therapeutic tests is that they do not prove anything incontrovertibly. They usually lack double-blind controls and statistical support. Perhaps the medical or surgical treatment could be also a sufficient psychotherapy. Perhaps during psychotherapy the organic condition has opportunity for spontaneous remission. Perhaps both treatments only cater to neurotic needs and the patient never gets well. In the latter case, have we proved a neurosis? Or that the therapy was incompetent? Or that the disease was an incurable one? However, when the patient makes a surprisingly gratifying response to either kind of therapeutic test and becomes rehabilitated after years of ailing disability and does not need the other therapy, then our skepticism should be recognized as only academic and unrelated to our primary calling, which is to restore health in the patient by rational means. In this respect a therapeutic test is preferable to persistent skepticism, indecision and therapeutic nihilism.

Conclusion

In neurosis the patient sacrifices his health unconsciously, thereby achieving escape from his responsibilities. Chronic complainers should not be shunted off as "neurotics" unless this mechanism is clearly in operation. Many of them have organic disease.

For a physician to be able to decide how much of an illness is organic and how much is neurotic, he needs a broad knowledge of the various possible courses each disease may

take in persons of various constitutions and what may be expected of treatments. He especially needs greater clarity in his concept of neurosis, and he needs criteria of differentiation. A diagnosis of neurosis should be proved, not made on suspicion only. A thorough exclusion of organic disease, diagnostically and therapeutically, is a part of the proof if the diagnosis of neurosis is to stand alone.

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Some Clinical Aspects of Nutrition and Infection

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FRED T. SAI

THE interrelationship between nutrition and infection is very complex and its mechanisms are poorly understood. However, it is necessary that practicing physicians be constantly aware of a relationship. Scrimshaw, Taylor and Gordon[1] have written an extensive review on this subject, and they put forward two concepts which assist in thinking of the subject—antagonism and synergism.

By *antagonism* they meant that malnutrition in the host is detrimental to the infective process and would therefore appear to assist the host. This situation exists mainly as regards some viral infections and does not concern us too much here.

Synergism implies that malnutrition in the host assists the infective process to be more severe in the host.

The nutritional status of a given subject at any given time is dependent on his previous diet as well as on the food he is currently eating. Thus chronic as well as acute or current faulty diet enters the discussion. Furthermore, the effects of undernutrition may be entirely different from those of malnutrition in which specific nutrients are lacking in an otherwise adequate diet.

The relationship between infection and nutrition is a two-way one. The infective process may directly or indirectly affect the individual's nutritional state, and the nutritional state appears to modify any infections that he encounters. It will be clear from the following discussion that whereas we can confidently state what happens to the nutrition of an infected individual, we cannot state the effects of nutrition on infection with anything like the same degree of confidence.

Only the clinical and epidemiologic work which would help to develop the subject has been cited in this paper, and practically all the animal and experimental work has been

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ignored. Those who are interested in getting better acquainted with this field may refer to the article by Scrimshaw, Taylor and Gordon and to the Symposium on Nutrition in Infections in the *Annals of the New York Academy of Sciences*.[2] Facts which have already appeared in standard textbooks are mentioned without any references.

Effects of Infection on Nutritional Status

Indirect effects—Anorexia and vomiting often accompany even minor infections. Viruses, bacteria and protozoa help to deprive patients of nourishment. At times, quite apart from anorexia, food is withheld from the patient in the mistaken notion that starvation will help recovery. In most sections of the tropics, as soon as a child has a little fever, solid foods, especially those rich in proteins, are removed from his diet. Purgatives are given, often drastic ones like castor oil and salts. All these factors work together to deprive a sick child of much-needed nutrients, and it is no wonder that infection almost invariably precedes the more acute manifestations of kwashiorkor. Other consequences may be dehydration and disturbed electrolyte metabolism.

Currently, very potent antibiotics are being used both wisely and unwisely by physicians and it is worth re-emphasizing that the broad-spectrum antibiotics may inhibit bacteria which synthesize vitamins in the intestinal tract. If the prepathogenic malnutrition of the patient has been prolonged and if care is not taken to give adequate vitamin cover, a patient may be precipitated into vitamin deficiency after an infective illness; this has been demonstrated for vitamin K in infants after administration of neomycin. Prolonged therapy with isoniazid precipitates pyridoxine deficiency. Some of these potent agents may remove an infection only to allow a previously mild bacterium or fungus a "softened field" for operation. A little-publicized effect of Guinea worm is that it may cripple a whole village during the plowing and planting season and consequently precipitate widespread undernutrition.

Direct effects—Trauma as well as acute and chronic infections lead to a negative nitrogen balance for varying lengths of time. Particularly severe losses of nitrogen have been known to occur in typhoid fever, pneumonia and tuberculosis. Attempts to reverse this negative nitrogen balance during the active phases of the diseases mentioned have failed. This simply means that a person previously marginal or malnourished as regards protein is likely to be precipitated into a frank protein-deficiency state by acute or chronic bacterial infection. This constantly happens in the case of kwashiorkor. There is little one can do to prevent the loss of nitrogen once the infection has started, but the quantity lost can be minimized with judicious feeding during the early active phases and the provision of a high-protein, easily digested diet during convalescence and the period immediately following.

Typhoid is a fairly common disease in some parts of the world, and one is impressed by the rapid loss of weight which follows an attack of typhoid, even in previously well-nourished persons. Given an adequate diet it may take weeks to regain the prepathogenic weight. But in some poor areas such loss of weight may never be made good. The complication of hemorrhage may lead to severe iron-deficiency anemia. The frequency with which a child previously diagnosed as having protein malnutrition or kwashiorkor turns out to have tuberculosis has long been known by pediatricians in the tropics. It is relatively easy to explain this association by chronic marginal protein intake coupled with prolonged negative nitrogen balance after internalization of the tubercle bacillus and throughout the early pathogenic stages of the disease process. A similar story can be told for shigellosis and almost all the bacterial illnesses which cause fevers.

Lest it be assumed that this applies only to bacterial infections, examples from viral, protozoan and helminthic infections may also be mentioned. Negative nitrogen balances follow the viral infections, too, and epidemics of measles in countries like Ghana and other developing areas are regularly followed by

what may be described as "epidemics of kwashiorkor."[3] Various protozoan illnesses, such as malaria and leishmaniasis, have all been shown to cause severe negative nitrogen balances and, in some instances, chronic gastric upsets, all of which lead to malnutrition of a severe degree. Hookworm accentuates protein and iron malnutrition by causing intestinal losses of blood. Pernicious anemia results from the fish tapeworm, *Diphyllobothrium latum,* which robs the host of vitamin B_{12}.

In all the situations discussed, there is no doubt that the presence of an infective agent either indirectly or directly prevents the host from taking nourishment, diminishes the absorption of what is taken, or increases losses. These effects may be minimal or perhaps not even demonstrable in a population as well nourished as that of the United States, but in people on marginal or suboptimal diets, they are readily seen and have to be treated.

Effects of Nutrition on Infection

The beneficial effects of nutrition on infection cannot be as easily substantiated as the converse effects. Most of the evidence in humans comes from epidemiologic studies. Some of these findings can be supported with animal experiments.

Of the bacterial infections, tuberculosis has been most intensively studied in the human being. Marche and Gounelle[4] have submitted evidence from France to show that increases in the mortality rate of tuberculosis during the war years from 1870 until the present can be attributed to subnutrition. In these studies it was impossible to remove the influence of overcrowding and the loss of moral and hygienic standards, all of which would influence both incidence and severity. However, unreported findings in West Africa support the fact that the poorly nourished populations have a much higher case fatality rate than those well nourished.

Clinically, one of the most significant aspects of this nutrition-infection interaction is perhaps the ease with which some so-called nonpathogenic bacteria are able to establish themselves and wreak havoc in the malnourished. Children with kwashiorkor are easy prey to pulmonary and gastrointestinal infections. Bacteriologic examinations on such children frequently yield reports such as "mixed growth of nonpathogens." It is not too theoretical a concept to view bacteria as forming a spectrum from the completely nonpathogenic to the actively pathogenic and that where the division occurs for a given individual may be determined, *inter alia,* by previous and present nutrition. Corollaries to this are ready development in malnourished children of severe complications, such as severe Vincent's infection and cancrum oris, stemming from ordinary organisms often found in the mouth and throat, and the high case fatality rates from whooping cough and other childhood illnesses.[3,5,6]

Of the protozoan diseases, amebiasis has received the most attention in the human being. Elsdon-Dew[7] reported the high incidence of fulminating intestinal amebiasis in the Bantu as opposed to the milder forms in the Indian and its near absence in the white population of South Africa. The differences were attributed to the better-balanced, protein-rich foods of the white and Indian population and the rather simple protein-poor, corn-based diet of the Bantu. The same worker found that the Bantu was more susceptible to severe intestinal amebiasis than the Negro of Lorenzo Marques; the latter has more fish and vegetables in his diet. In Ghana, I have been impressed by the fact that those who generally present with acute and severe intestinal amebiasis are emaciated and have been subsisting on very poor diets. The emaciation antedates the amebiasis.

Alexander and Meleney,[8] working in Tennessee, reported finding amebas in the feces of 40 per cent of the population in two communities, yet clinical amebiasis was common only in the community where there was little milk or vegetables in the diet. I am impressed by the fact that sufferers from amebiasis from the more rural and poorer areas of Ghana have a more serious intestinal disease and are often obviously malnourished. This contrasts sharply with the rather long drawn-out, relatively mild dysentery found in the better-fed

populations in towns and larger villages.

During the Korean campaign, doctors found that amebiasis among troops reached epidemic proportions during periods of food shortage.[9] In a therapeutic trial, 11 out of 66 soldiers recovered on good food with no drugs. This cannot be accepted at face value since spontaneous recovery from amebiasis has been known to occur.

Work on helminthiasis in the human being is restricted. It is well known that hookworm disease does not develop in the well-nourished individual despite the fact that he may carry a large worm load. The only adequate explanation is that enough food is being supplied to feed both worms and host. White et al.[10] gave Peruvian children, anemic from hookworm, daily supplements of iron and showed that in spite of the presence of the worms the hemoglobin levels went up. This illustrates that even during the pathogenic phase, improvement in nutrition may affect the balance between parasites and host to the latter's advantage. It has been noted for some time now that a high proportion of underweight and undernourished children have heavy loads of *Ascaris* and the various complications of ascariasis. Persons familiar with onchocerciasis are impressed by the higher incidence of "onchocercal blindness" in an affected population subsisting on a diet inadequate in calories, vitamin A and riboflavin than in those with an adequate diet. Deficiencies in both vitamin A and riboflavin affect the eye, and so it is not surprising that a synergism is found between them and onchocercal disease of the eye. These differences are very striking when one compares affected populations in the north of Ghana and their fish-eating counterparts on the southern shores of the river Volta. The rate of blindness is very high in the poor northern region.

The role of nutrition in the natural history of infections has been debated for a long time and the debate will continue. Advocates of vitamins or special diets as panaceas for infective illnesses do the subject a disservice. At the same time, those who discount experimental findings in the belief that the degree of starvation or of malnutrition required to make a difference is too extreme to exist in the human being are obviously being parochial. In many parts of the tropics people are subsisting on diets often as poor as those used in the laboratories and for much longer relative periods. Who in the United States can conceive of a child eating a food which contains 0.5 per cent of poor protein as the only source of nitrogen? Yet this happens among cassava eaters; and the degree of protein malnutrition is as severe as any that has been produced in laboratories.

In addition to poor food, an unsanitary environment and lack of medical facilities cause children and adults to harbor an army of pathogenic bacteria, protozoa and helminths. These have to be fed, and directly or indirectly they reduce the food available to the host. Dubos and Schaedler's[11] findings in pathogen-free mice are pertinent at this point. The pathogen-free mice continued to grow on poor diets on which mice containing pathogens had stopped growing. At the risk of being accused of extrapolating from mice to man, one can say that some such situation is likely to exist in man, too. In well-fed communities there is enough for both host and parasites, but this happy situation does not exist in many parts of the world.

Conclusion

The effects of infection on nutrition are well documented in the human being. The more complex effect of nutrition on infection is yet to be well established, and the mechanisms involved can only be conjectured at present. There is little doubt that organisms compete with host cells for nutrients, and the balance between host and parasite depends on the amount of nutrient available, how important is the deficient nutrient to host or parasite nutrition, and how well adapted is host or parasite to compete for nutrients in short supply. Such an interrelationship will explain why some parasites fare poorly in the face of malnutrition (e.g., viruses are on the whole not successful in the face of severe protein undernutrition in the host), while the majority completely overwhelm the malnourished host. Even in the absence of evidence

that good nutrition is helpful in staving off or recovering from all infective illnesses, there is little doubt that practically all these diseases lead to a negative nitrogen balance and, therefore, good nutrition would appear to be always desirable.

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Self-help Devices:

Homemaking: Kitchen Area Work Seat and Work Surfaces

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THE Functional Home for Easier Living, described in the December 1960 issue, is meant to serve as a guide to anyone needing to build or adapt a home to the specifications given. However, adjustments in the home to compensate for loss in physical dexterity can be approached on a much smaller scale in the patient's existing environment. This homemaking series of six articles will illustrate changes requiring comparatively little basic alteration and expense.

Since the major work activity of the homemaker is centered in the kitchen, this article will describe some of the problems encountered in this area by the disabled person. Homemaking analysts have shown that most jobs can be accomplished from a sitting position, and wheel-chair patients have confirmed this. In the interest of energy conservation, however, all homemakers are urged to sit whenever possible. Of prime importance is the selection of a work seat which provides a comfortable sitting arrangement for the task at hand and a work surface at a convenient height.

The Work Seat

The ideal sitting arrangement is a chair or stool, depending on the height of the working area, which gives ample support to the entire body, with support at the lower back so that shoulder and elbow movements are not inhibited. The feet should rest squarely on the floor or on a footrest. Often it is necessary to home-devise footrests when using higher seats.

*Supported at the Institute by the Arthritis and Rheumatism Foundation.

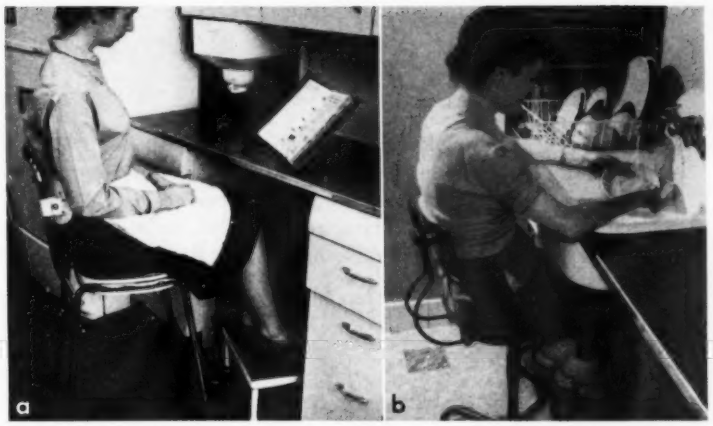

FIGURE 1. a. The patient's feet should rest squarely on the floor or on a footrest that fully supports the feet, with no pressure behind the knees and with the knee angle greater than 90 degrees.

b. This chair is adjustable and is designed for commercial purposes. Its 10 in. variation from standard-height chairs makes it adaptable to different work heights, and the back rest is also adjustable. The foot support, however, is inadequate and does not adjust to the varied seat heights.

Work Surfaces

With the patient comfortably seated, the next concern is the relation of the seat height to the working level. Ideally, a work surface should permit the homemaker to sit erect but relaxed, with the elbows close to the body and the work surface below the point of the elbow and with adequate clearance for the knees and lower legs.

The homemaker in a wheel chair often finds it difficult to approach working surfaces and to maneuver the chair into a comfortable position under the sink, table, etc.

FIGURE 2. Convenient work surfaces can be easily improvised, such as (a) a table on wheels; (b) a drop-leaf shelf; (c) an adjustable ironing board, and (d) a lapboard.

Sink and Stove Areas

Work at the sink occupies a considerable portion of the homemaker's time. It should be remembered that the work is done mostly at the bottom of the sink. The accepted method for testing for the correct height is to sit or stand correctly balanced with elbows relaxed but extended. In such a position, the palms of the hands should rest comfortably on the sink floor.

The stove, too, may be too high for convenience. This problem may be solved as illustrated in figure 5.

FIGURE 3. When the sink is too low, a rack can be used to raise a dishpan or other container to the desired work height.

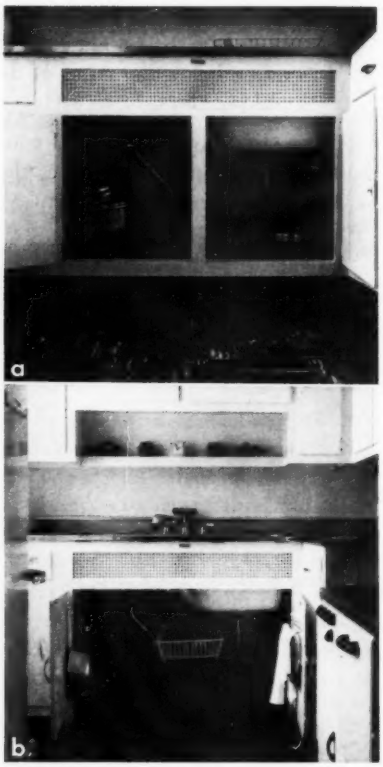

FIGURE 4. a and b. If the sink is too high, it is sometimes desirable but not always feasible to lower the entire unit. The cabinet shown in (a) was altered by removing the subbase and the vertical strip (b). With the doors open, clearance is obtained for the legs.

FIGURE 5. If the stove is too high for the homemaker who is in a wheel chair, it should be lowered if possible. An alternative is the substitution of several electric appliances which can be placed at good working levels elsewhere in the kitchen.

CLINICAL STUDY

Steroid Therapy in Cases of Allergic Disease

NATHAN E. SILBERT*

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This report covers a study of 83 cases of allergic disease in which dexamethasone was administered.

Results of treatment were evaluated on the basis of subjective symptoms and of the effect of the drug on the results of tests for pulmonary ventilation and volume.

In almost all cases, relief was obtained by the end of the second day after administration of the drug was started.

NATHAN E. SILBERT

CURRENT medical literature contains many reports on the use of steroids in the treatment of allergic diseases. It should be realized, however, that these drugs are not a panacea. In 1952, I said that the advisability of using steroids in cases of allergic disease should be considered, especially in cases in which a respiratory infection is superimposed on a pre-existing allergic disease.[1] In such cases, the use of steroids may produce temporary relief of the allergic symptoms without having any effect on the respiratory infection.

Since steroids are available for the treatment of allergic diseases such as bronchial asthma, severe pollenosis, intractable perennial nasal allergy, acute exacerbations of eczema, and other allied conditions, certain pertinent factors should be considered in order to evaluate the proper role of the steroids in the treatment of these diseases.

It is well known that corticosteroids prevent the formation of antibodies. However, if no antibodies are present, union between antibodies and antigen cannot occur. Steroids have no effect on the antigen-antibody reaction. There is no reason why steroids cannot be used satisfactorily in the treatment of status asthmaticus, severe episodes of seasonal or perennial nasal allergy, acute exacerbations of eczema, and severe contact dermatitis due to poisoning with ivy, oak or sumac, and due to industrial oils, soaps, etc.

Since the report by Hench, Kendall, Slocumb and Polley,[2] a constant search for analogs of cortisone has continued in research laboratories. In 1953, Fried and Sabo[3] produced 9-alphafluorides and the halogen atom at the C-9 position, which resulted in an increase in the biologic activity of the steroid. However, since sodium retention became a critical factor, atom substitution continued.

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TABLE 1

TYPE OF ALLERGIC DISEASE AND AGE AND SEX OF PATIENTS

TYPE OF ALLERGIC DISEASE	CASES	SEX		AGE (YEARS)
		M	*F*	
Seasonal hay fever	21	8	13	6 to 71
Perennial nasal allergy	7	2	5	18 to 63
Contact dermatitis				
Due to plants (ivy, oak and sumac)	5	4	1	7 to 21
Industrial	2	2		35 to 54
Asthma				
Perennial (due to dust, mold, bacteria and pollen)	12	8	4	7 to 78
Infectious	8	6	2	35 to 73
Seasonal (pollen in nature)	24	10	14	6 to 78
Miscellaneous skin allergy associated with other pathologic conditions	2	2		26 to 37
Diffuse angioedema and urticaria (undetermined nature)	2	1	1	19 to 42
TOTAL	83	43	40	

The substitution of the methyl group for the hydroxy-7 group at the C-16 position resulted in the development of a hydroxyl group at the C-16 position. This produced dexamethasone (GAMMACORTEN®), a drug which was capable of eliminating to a considerable degree the sodium-retaining effect of the compound with the halogen at the C-9 position. On a milligram for milligram basis, this new steroid analog is more potent than cortisone, hydrocortisone, prednisone and prednisolone. In his address at the 1960 meeting of the American College of Allergists, Kendall said that dexamethasone is 33 times more potent than cortisone. In addition, it causes considerably less retention of sodium.

It may be pertinent to say a word about the hormones secreted by the suprarenal cortex and the effect of the pituitary body in producing the ultimate end product. The medulla of the suprarenal gland produces epinephrine, which stimulates the anterior lobe of the pituitary body to produce the adrenocorticotropic hormone (ACTH), which in turn stimulates the suprarenal cortex to produce the corticosteroids. The secretions of the suprarenal cortex may be classified as the androgenic hormones, which produce the urinary 17-ketosteroids, and the hydroxycorticosteroids (compounds E and F), which in turn influence (1) the blood eosinophils and lymphocytes, (2) the production of antibodies, and (3) histamine, histaminase, the histidine factors and aldosterone, which influences electrolyte balance and the general alarm syndrome of Selye.

Twenty-nine steroids have been extracted from the suprarenal cortex. Of the synthetic steroids, the most potent and interesting is dexamethasone.

Material and Method of Study

This report is based on a study of 83 cases of allergic disease in which dexamethasone (Gammacorten)* was administered. Table 1 shows the age and sex of the patients and the type of allergic disease that was present. Routine tests for allergic diseases were used in all cases, and the blood and urine were examined. In the 44 cases of asthma, tests for pulmonary function were used. These tests included determination of the timed vital capacity and the various components of the total lung capacity.

*The dexamethasone used in this study was supplied by the Ciba Pharmaceutical Products, Inc., through the courtesy of Drs. J. Harold Walton and Frank J. Vinci. This firm supplies dexamethasone (Gammacorten) in the form of tablets containing 0.75 mg. of the drug. Some other firms supply dexamethasone in the form of tablets containing 0.50 and 0.75 mg. of the drug.

TABLE 2

RESULTS OF ADMINISTRATION OF DEXAMETHASONE IN 83 CASES OF ALLERGIC DISEASE

ALLERGIC DISEASE	CASES	COMPLETE CESSATION OF SYMPTOMS	EXCELLENT RELIEF	GOOD PROGRESS*	LITTLE OR NO BENEFIT
Seasonal hay fever	21	4	10	5	2
Perennial nasal allergy	7		4	1	2
Contact dermatitis					
Due to plants	5	1	3	1	
Industrial	2		1	1	
Asthma					
Perennial	12	2	3	5	2
Infectious	8†		2	3	3
Seasonal (pollen in nature)	24	6	13	4	1
Miscellaneous skin allergy associated with other pathologic conditions	2		1	1	
Diffuse angioedema and urticaria (undetermined nature)	2		1	1	
TOTAL	83	13	38	22	10

*Better than 75 per cent relief of symptoms.

†In five of these eight cases, adjunctive antibiotic therapy was needed in order to produce complete relief of symptoms. In three of the eight cases, the administration of an antibiotic in conjunction with dexamethasone actually did produce some relief although the administration of dexamethasone alone did not do so.

The dosage schedule was as follows:

For adults:

4 tablets daily for four days.
3 tablets daily for next four days.
2 tablets daily for next three days.
1 tablet daily for next five days.
1 tablet every other day for next 12 days.

For children:

3 tablets daily for four days.
2 tablets daily for next three days.
1 tablet daily for next five days.
½ tablet every other day for next 12 days.

In a few cases in which adult patients failed to respond by the end of the second day after administration of the dexamethasone was started, 5 tablets were administered daily for four days. Then the usual dosage schedule was resumed. It rarely was necessary to administer more than 5 tablets per day to adults or more than 3 tablets per day to children.

TABLE 3

SIDE EFFECTS OF DEXAMETHASONE

SIDE EFFECTS	CASES
Increase in body weight	6
Abdominal distention	1
Gastric distress	2
Nausea	1
Vomiting	1
Moon face	3

Results

Table 2 shows the results of treatment with dexamethasone in the 83 cases. The results were evaluated on the basis of the relief of the subjective symptoms and on the basis of the effect of the drug on the results of tests for lung ventilation and lung volume. In almost all of the cases, relief was obtained by the end of the second day after the administration of the drug was started. Side effects occurred in only a few cases (table 3), and they disappeared in a short time after the administration of the drug was discontinued.

TABLE 4

RESULTS OF TESTS FOR LUNG VENTILATION AND LUNG VOLUME IN CASE 1

TEST	FEBRUARY 2, 1960*	FEBRUARY 4, 1960
Tidal volume, cc.	916	785
Inspiratory reserve volume, cc.	491	1,112
Expiratory reserve volume, cc.	0†	164
Inspiratory capacity, cc.	1,406	1,897
Vital capacity, cc.	1,373	2,060
Functional residual capacity, cc.	2,335	2,932
Total lung capacity, cc.	3,708	4,829
Residual volume, cc.	2,335	2,767
Residual volume, percentage of total lung capacity	63	57
Helium washout, minutes	9	9

*Before administration of dexamethasone was started.

†Vital capacity was less than inspiratory capacity.

The respiratory rate was six per minute on February 2 and nine per minute on February 4.

TABLE 5

RESULTS OF TESTS FOR LUNG VENTILATION AND LUNG VOLUME IN CASE 2

TEST	FEBRUARY 26, 1960*	MARCH 12, 1960
Tidal volume, cc.	490	555
Inspiratory reserve volume, cc.	554	585
Expiratory reserve volume, cc.	683	1300
Vital capacity, cc.	1,692	2,440
Functional residual capacity, cc.	4400	4700
Total lung capacity, cc.	5,030	5,660
Residual volume, cc.	3,280	3,260
Residual volume, percentage of total lung capacity	65	57
Helium washout, minutes	7	9

*Before administration of dexamethasone was started.

Case Reports

I shall report three cases briefly in order to illustrate the effect of the administration of dexamethasone on the results of tests for lung ventilation and lung volume.

Case 1—A 49 year old woman first was observed on February 2, 1960, because of severe bronchial asthma that had been present for 10 days. She had consulted several physicians, but the medications that they had prescribed had not produced any relief. Administration of dexamethasone was started according to the schedule previously described. Table 4 shows the effect of the drug on the results of tests for lung ventilation and lung volume.

Case 2—A 74 year old man was observed on February 26, 1960, because of a severe attack of bronchial asthma which had continued unabated for the previous three weeks. The history revealed that the patient had had

TABLE 6

RESULTS OF TESTS FOR LUNG VENTILATION AND LUNG VOLUME IN CASE 3

TEST	APRIL 15, 1960*	APRIL 20, 1960
Tidal volume, cc.	654	654
Inspiratory reserve volume, cc.	948	1,505
Expiratory reserve volume, cc.	785	229
Inspiratory capacity, cc.	1,602	2,158
Vital capacity, cc.	2,387	2,387
Functional residual capacity, cc.	2,951	2,230
Total lung capacity, cc.	4,553	4,388
Residual volume, cc.	2,266	2,001
Residual volume, percentage of total lung capacity	50	45
Helium washout, minutes	9	9

*Before administration of dexamethasone was started.

The respiratory rate was six per minute on April 15 and seven per minute on April 20.

bronchial asthma for 12 years. The longest period of efficacy of previous treatment never had exceeded 24 hours. Administration of dexamethasone produced complete relief in 24 hours, and the administration of the drug was discontinued. Table 5 shows the effect of the drug on the results of tests for lung ventilation and lung volume.

Case 3—A 45 year old man first was observed by me on April 15, 1960, because of a severe attack of bronchial asthma. The patient had had bronchial asthma for 12 years. He had been in a sanatorium for a year and a half, and a pneumothorax had been induced on several occasions.

The present attack had been present for two weeks, and it had failed to respond to various types of medication that previously had produced relief. Administration of dexamethasone produced relief in 48 hours. Table 6 shows the effect of the drug on the results of tests for lung ventilation and lung volume.

Comment

In my experience, dexamethasone has proved to be a valuable drug in the treatment of allergic diseases. Although steroids are effective drugs, they are dangerous. In cases in which a steroid is administered, extreme care must be taken to determine the proper dose, and the patient should be observed carefully for the development of side effects. The patient's tolerance for the drug must be carefully evaluated, and the dose administered should be the smallest one that will produce the desired effect. This, of course, requires strict observance of the patient by the physician.

If the physician remembers that steroids are intended for short-term use, complications and side effects will be minimal. In my practice, it has been almost axiomatic to use steroids only for short-term or emergency therapy, and it only rarely has been necessary to break this rule. Once the acute episode of the disease has been controlled, another drug may be used to maintain the *status quo*, but it should not be a steroid.

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CLINICOPATHOLOGIC CONFERENCE

Report From Veterans Administration Hospital, Hines, Illinois

Edited by William J. Donnelly, M.D., Chief, Section of Hematology

Case Report

A MARRIED white man was 69 years old at the time of his last admission to Hines Veterans Administration Hospital in January 1959. In 1951, it was found that he had diabetes. He was moderately obese at that time, but soon achieved a stable, normal weight of 140 lb. He took 20 units of NPH insulin daily, tested his urine frequently, and consulted his physician regularly.

He was first admitted to Hines in June 1957, because of a gangrenous left second toe. He had intermittent nocturnal leg cramps but no claudication, and for several years had stasis dermatitis and recurrent ulcers of the legs. Except for the gangrenous toe, examination was not remarkable. Blood pressure was 140/90 mm. Hg, cardiac murmurs were not heard, and an electrocardiogram was interpreted as normal except for sinus arrhythmia. A moderate amount of pulmonary emphysema was present, but two chest x-rays were otherwise normal. Plasma proteins, nonprotein nitrogen and hemogram were all normal, and urinalysis was negative except for glycosuria.

The patient was treated with a left lumbar sympathectomy and amputation of the gangrenous toe. Postoperatively he had fever and evidence of infection in the left foot, from which *Pseudomonas* was cultured. Drainage and antibiotic therapy were unsuccessful and a midthigh amputation was performed subsequently. The patient incidentally had a furuncle on the left wrist which was incised and drained. During his hospital course he was easily managed with NPH insulin (35 to 45 units daily).

He did well after his dismissal from the hospital in December 1957, until January 1959, when he was readmitted because of intermittent fever, increasing sleepiness, anorexia, nausea, vomiting and weight loss for several weeks. Control of the diabetes had been poor, and the patient frequently had omitted insulin.

He was extremely lethargic, confused and somewhat disoriented, but afebrile. Blood pressure was 180/80 mm. Hg. The lungs were normal except for emphysema. A systolic murmur was heard at the apex, and a systolic murmur at the base radiated into the neck. The second aortic sound was greater than the second pulmonic sound; rhythm was regular, with a rate of 74. The liver was palpable 7 cm. below the right costal margin and had a firm nontender edge; the level of the upper border of hepatic dullness was not described. The abdomen was otherwise normal. There was a small stasis ulcer over the right lateral

malleolus. Pulses in the right foot were absent.

Laboratory data—At the time of admission the leukocyte count was 16,100 with 85 per cent neutrophils. The hemoglobin level was 8.5 gm., the hematocrit reading was 24 per cent, and the reticulocyte count was zero. Urinalysis disclosed 1+ albuminuria, 4+ glycosuria and 4+ acetonuria; specific gravity was 1.018. The blood sugar level was 334 mg., nonprotein nitrogen 47.5 mg., carbon dioxide 20.8 mEq., chlorides 89 mEq., sodium 129 mEq. and potassium 4.5 mEq. The blood acetone test gave a positive result of 1+, the cephalin-cholesterol flocculation test was negative, and thymol turbidity was 3 units. Total bilirubin was 0.7 mg., total protein 5.8 gm., albumin 2.2 gm. and alkaline phosphatase 5.1 Bodansky units. An electrocardiogram was abnormal and compatible with electrolytic imbalance. A chest x-ray revealed a 25 per cent increase in cardiac diameter but clear lung fields.

The patient received the appropriate therapy for diabetic acidosis. Acetonuria vanished rapidly, and serial serum electrolyte determinations remained within normal limits. Subsequent determinations of blood urea nitrogen showed levels between 23 and 49 mg., increasing during the hospital stay; however, serum creatinine levels remained within normal limits (1.2 to 1.4 mg.).

Although the diabetes was controlled easily with 15 to 25 units of NPH insulin daily, the patient remained sleepy and lethargic. He improved slightly during the first week. Repeated leukocyte counts ranged from 5300 to 15,000 with 80 to 84 per cent neutrophils and the remainder lymphocytes. The hemoglobin level varied from 7 to 9 gm. despite transfusions given on the fourteenth and seventeenth hospital days. On the fourteenth hospital day a sternal marrow aspirate revealed a slightly hypocellular marrow, normal megakaryocytes, a ratio of nucleated red blood cells to white blood cells of 1 to 4, normoblastic erythropoiesis, slightly toxic granulopoiesis, slightly increased eosinophils and plasma cells, and a moderate increase in reticular cells.

The patient had fever varying from 100 to 101.5° F. from the sixth through the eighth hospital day. Afterward he was afebrile until a low-grade fever returned on the twenty-second day. His temperature was 103° F. on the twenty-seventh hospital day. At this time the urinary sediment was loaded with pus cells and 1+ albuminuria was present. *Proteus mirabilis* was cultured from the urine. He was treated with GANTRISIN®, 4 gm. a day, and became afebrile in a very short time. A subsequent urinalysis showed very few white cells per high-power field and no albumin. After 10 days the dosage of Gantrisin was reduced to 0.5 gm. twice daily.

Stools were negative for occult blood on two occasions and slightly positive once. An upper gastrointestinal x-ray series, an intravenous pyelogram and a barium-enema study were normal.

Throughout his hospital stay the patient progressively lost weight, and generalized weakness increased. He had periods of confusion and disorientation alternating with alertness. Urea clearance was 47.5 by the maximum-flow formula on the forty-fifth hospital day. On the forty-sixth day, oral iron therapy was started. On the fiftieth day the patient again became febrile. Urinalysis revealed 2+ albuminuria and 6 to 8 white cells and 12 to 15 red blood cells per high-power field. Urinary culture at this time yielded *Pr. mirabilis* and hemolytic *Staphylococcus aureus*, coagulase-positive (both resistant to all antibiotics tested). Blood pressure was 140/80 and the pulse rate was 120. The heart was enlarged, there was a systolic murmur at the apex, the lungs were clear, and the liver was unchanged in size. A chest x-ray two days later showed a patchy infiltrate in the right base. Gantrisin (0.5 gm. twice a day) was continued until the day before the patient died, when penicillin was administered. Intravenous fluid therapy also was started, but the patient remained febrile and slipped deeper into coma. He died on the fifty-fifth hospital day.

Discussion

DR. ALEXANDER P. REMENCHIK (clinical investigator, research service): In my opinion, clinical medicine is a scientific discipline be-

cause the clinician applies the scientific method to the study of patients. He starts with observations (historical, physical and laboratory), formulates a hypothesis (diagnosis), makes predictions (specific therapy), and designs an experiment to test his predictions (additional laboratory data and observations of the course of the disease).

We will start with the historical observations. The patient was a man 69 years old who was known to have had diabetes since 1951. He was first admitted to this hospital in June 1957. Despite good control of the diabetes, gangrene developed—a common complication of diabetes. Conventional treatment was successful. His subsequent clinical course was not unusual until January 1959, when he was readmitted with a history of fever, lethargy, anorexia, nausea, vomiting and weight loss of several weeks' duration. The clinician believed the patient's diabetes was poorly controlled.

The following observations were made during the physical examination: (1) "emphysema," which I will assume meant a barrel chest; (2) the liver was palpable 7 cm. below the right costal margin (the width of the liver is not described, and hepatomegaly was not found during the first admission); I will assume hepatomegaly was present and the liver was not simply palpable because of downward displacement by a flat diaphragm; (3) the heart was slightly enlarged and murmurs were heard over the precordium.

The initial laboratory data were typical of diabetic acidosis.

First I will consider the fever. Kiefer and Laird have defined "prolonged fever" as fever that lasts more than two weeks. They have found at the Boston City Hospital that the most common causes of prolonged fever are tuberculosis, endocarditis and neoplasms—particularly neoplasms of the kidney, gastrointestinal tract, bones and nose. A simple classification of the causes of fever would include (1) bacteremias, associated with (a) localized infections—those *with* abscess formation (e.g., appendiceal abscess or perinephric abscess) and those *without* abscess formation (encephalitis, hepatitis, pyelonephritis); except for the presence of pus in the urine, we have no specific localizing signs indicating the presence of a large abscess in this patient; (b) specific infections such as malaria, brucellosis, tularemia, salmonellosis, etc.; there are no historical observations to suggest any of these; (2) toxic and allergenic agents such as drugs, foreign proteins, products of tissue necrosis; there is no recent history of drug ingestion other than insulin; (3) diseases of the blood and blood-forming organs, tumors, and the collagen diseases, of which there are no clinical signs here. Therefore, I conclude that a bacteremia was responsible for this patient's fever.

The next observation I will discuss is weight loss. The conditions that most commonly cause weight loss are neoplasms, thyrotoxicosis, infections and collagen diseases. The extent of the patient's weight loss is not described. This may be a significant clue in certain situations where weight loss is extreme, as in carcinoma of the stomach. I do not think we can learn anything from the weight loss except that the man was chronically ill.

Confusion and lethargy imply nervous system disease. Is this diffuse or local? The comments in the protocol suggest diffuse disease. There were no signs of peripheral neuropathy, no focal central nervous system signs, and no meningeal or cerebellar signs. Therefore, I would conclude that the disease was limited to the cortical areas. What type of central nervous system disease is limited to the cortical areas? The degenerative and demyelinating diseases come to mind, but there is no compatible historical evidence. Functional changes capable of producing these phenomena are increased intracranial pressure due to pseudotumor cerebri, lead or hypertensive encephalopathy, and metabolic disorders such as hyperthyroidism and uremia. On numerous occasions the creatinine, nonprotein nitrogen and blood urea nitrogen were within normal range or moderately elevated. The description of the patient's physical condition does not suggest hyperthyroidism. The next big category is infection, and the type of infection that would produce diffuse changes in the cerebrum would be encephalitis.

Another finding to consider is the hepatomegaly. For the sake of discussion I will assume that the liver was not simply displaced inferiorly into the abdomen as a result of pulmonary emphysema. What are some of the causes of hepatomegaly? Congestion of the liver due to heart failure or obstruction of the hepatic veins is a common cause; however, congestive hepatomegaly seems unlikely since the liver was not tender nor did it change during the course. Obstruction of the common bile duct is readily excluded in the absence of jaundice. Neoplastic involvement seems unlikely; no nodules were felt. Cirrhosis is a remote possibility without a history of jaundice or of alcohol intake. Fatty infiltration of the liver is an excellent possibility in a diabetic. Amyloidosis associated with the chronically infected lower extremities is not likely. Hemochromatosis is suggested by the hepatomegaly and diabetes, but skin changes were not described.

What about the murmurs? The heart was enlarged and murmurs were heard. What are the possible causes of these findings? Preexisting syphilitic, rheumatic or congenital valvular disease in this 70 year old man can be excluded because of the absence of murmurs during his previous hospitalization. What about acute rheumatic fever? Acute rheumatic fever does occur at this age; however, the patient did not have joint symptoms. What about the endocarditides? We know they are associated with nonspecific murmurs; however, this diagnosis would not explain the extracardiac symptoms and signs. Myocardial disease? We know that anemia with dilatation of the heart due to myocardial disease is frequently associated with murmurs. Infections such as diphtheria and trichinosis are not historically implicated. Intoxications, nutritional disturbances and beriberi again are not suggested historically. Myocardial disease secondary to coronary atherosclerosis seems unlikely without a history of an infarct or of angina. Amyloid disease usually is associated with severe congestive heart failure or a nephrotic syndrome; involvement of the brain in amyloidosis is extremely rare. When amyloid disease does involve the nervous system it usually involves the peripheral nerves. Collagen diseases and hemochromatosis may produce myocarditis, but I will reject these for the reasons I mentioned previously.

Are there any clues in the laboratory data? A presumably normochromic normocytic anemia associated with a hypocellular marrow may be secondary to several diseases. Hypothyroidism and hypopituitarism can produce normochromic normocytic anemia with a hypocellular marrow. Uremia may do the same, but the nonprotein nitrogen and blood urea nitrogen were only moderately elevated. Toxic agents or drugs are not implicated historically. Lastly, chronic infections usually are associated with a normochromic normocytic anemia and a hypocellular marrow.

What about the renal findings? On admission the specific gravity of the urine was 1.018. I am informed that subsequent random examinations of the urine revealed specific gravities of about 1.011 or 1.012. However, the urea clearance test done shortly before the patient died was normal for a 70 year old man. Proteinuria is not specific and therefore is not helpful. White cells in the urine may be an indication of systemic disease such as a collagen disease or of a local infection. A positive bacterial culture was obtained, but this was not a quantitative culture; the absence of a quantitative culture limits us. The presence of red cells in the urine suggests the following possibilities: (1) neoplasm, (2) tuberculosis, (3) hypertensive vascular disease and (4) glomerulitis. The intravenous pyelogram was described as normal, and therefore I will eliminate tuberculosis and neoplasm. The absence of a history of high blood pressure and a recorded normal blood pressure on two occasions when the patient was admitted to the hospital eliminate hypertensive vascular disease. I will conclude that the hematuria was due to glomerulitis. Now what are the causes of glomerulitis? They are bacterial endocarditis and collagen diseases.

Two more findings are hyperglobulinemia, of slight degree and consistent with a diagnosis of chronic infection, and the melena in the latter part of the course, which suggests an ulcer in the upper gastrointestinal tract.

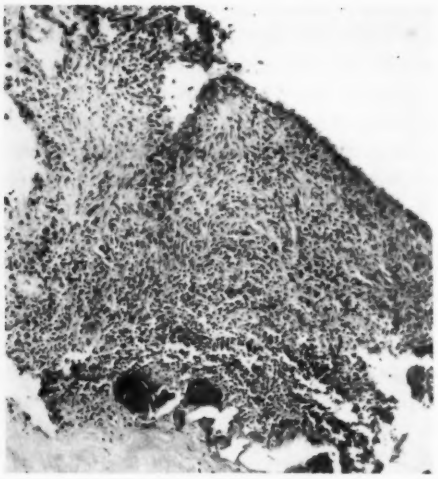

FIGURE 1. Photomicrograph showing hyalinization of the mitral valve with a large vegetation, at the base of which are two clumps of bacteria.

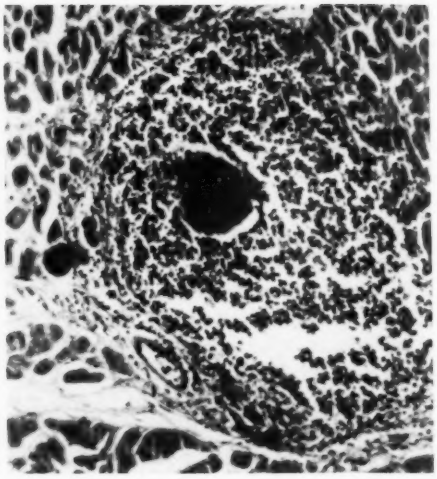

FIGURE 2. Photomicrograph showing a small septic infarct in the myocardium.

What was the pathogenesis of this ulcer in view of the normal gastrointestinal x-rays? I believe it was secondary to the central nervous system lesion.

In summary, then, what are the significant facts? The patient, a 69 year old man, had fever for a number of months. He had murmurs, red cells in the urine, and evidence of central nervous system disease. I think the only logical diagnosis is subacute bacterial endocarditis. Therefore, I will predict that there were vegetations on the heart valves, coronary atherosclerosis, glomerulitis and cerebritis.

DR. WILLIAM E. FREDERICK (assistant chief, radiology service): A chest film in 1957 was normal. In January 1959 a posteroanterior chest x-ray demonstrated enlargement of the heart estimated as a 25 per cent increase in transverse diameter. Upper and lower gastrointestinal x-ray series in January 1959 were entirely normal. Intravenous pyelography did not reveal abnormalities.

DR. DONNELLY: Dr. Remenchik, why do you think that the diagnosis of bacterial endocarditis was not considered clinically?

DR. REMENCHIK: Endocarditis is often a difficult diagnosis for the individual physician following the patient to make. Reviews from numerous institutions indicate that people frequently do not consider the diagnosis. This case in some respects was atypical. The older patient usually presents with congestive heart failure or uremia; the presentation with cerebritis is unusual.

DR. DONNELLY: Most of the symptoms which brought the patient to the hospital were easily explained by a long-standing diabetic acidosis. The acidosis probably had been precipitated by the urinary tract infection. We were disturbed when the patient did not do well after control of his carbohydrate metabolism. He continued to lose weight, and debility increased. We searched for other causes but were unsuccessful in establishing the correct diagnosis. We thought that the anemia was due to the azotemia, but also suspected an occult carcinoma.

DR. MYRON E. RUBNITZ (chief, laboratory service): Dr. Remenchik, what do you mean by cerebritis?

DR. REMENCHIK: Cerebritis literally means inflammation of the cerebrum. Encephalitis is the more conventional term and is the one I should use. Pathologically there is a perivascular infiltration of mononuclear cells and perhaps small embolic abscesses, but I believe

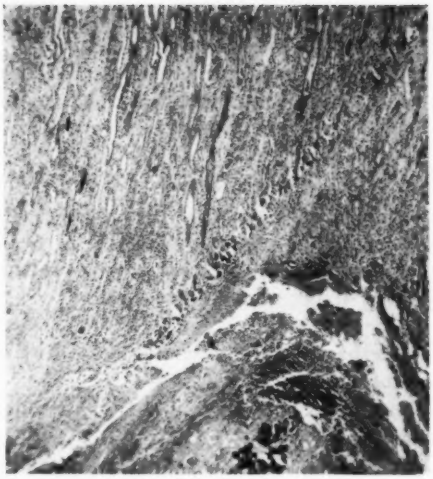

FIGURE 3. Photomicrograph showing a necrotic renal papilla with a number of small clusters of bacteria.

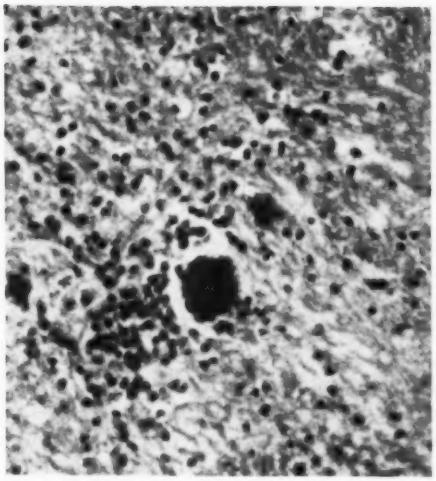

FIGURE 4. Photomicrograph showing a small septic infarct in the brain.

the predominant lesion is one of perivascular infiltration by mononuclear cells.

DR. RUBNITZ: Then you assume that this cerebral lesion was secondary to the heart lesion, not an independent condition?

DR. REMENCHIK: That's right.

DR. ARMAND LITTMAN (chief, medical service): I would like to compliment Dr. Remenchik on his courage for taking the point of view that the diabetes is an irrelevancy. We will soon find out if his courage is justified.

I too reacted to the term "cerebritis," Dr. Rubnitz. It is perhaps a convenient kind of shorthand. I see no more objection to it than to "encephalopathy" or "brain syndrome" or any of the others. I would merely like to remark that in the poorly controlled diabetic there are a number of phenomena specific to that circumstance, which should be mentioned.

It is stated in the protocol that the patient frequently had omitted insulin. When a patient omits insulin frequently, it is not always a matter of stupidity, indolence or a suicidal tendency. Frequently the patient who omits insulin does so because he has had a number of reactions. It is extremely common for patients receiving the combining forms of insulin to have hypoglycemia that does not produce the typical sweating and shakiness, hunger, and general feeling of "unwellness" typically associated with the rapid fall of blood sugar after regular insulin. Diffuse cortical damage often occurs in a diabetic who has frequent hypoglycemic episodes, even when they are not recognized clinically. Such brain damage may be manifested in many ways. Lethargy is a fairly common manifestation; personality changes are another. This lethargy is the kind that experienced psychiatrists can recognize in a patient who is "burned out" from repeated shock therapy.

Postmortem Findings

DR. RUBNITZ: At autopsy the findings were primarily those of complications of diabetes mellitus.

The heart weighed 410 gm. There were numerous ragged, friable, large vegetations on the mitral valve and a perforation measuring 1 by 0.4 cm. in the anterior leaf of the mitral valve. Even grossly, these findings are pathognomonic of *acute*, rather than *subacute*, endocarditis. Microsections of the mitral valve showed that these vegetations were composed of fibrin and numerous bacteria. Contrast this lesion with the lesion of rheumatic endocarditis, in which there is a smooth valvular surface with intact endothelial lining. Other micro-

sections of the mitral valve showed, in addition, an extensive inflammatory infiltrate and some hyalinization of the valve wall itself (figure 1). At higher magnification the coccal nature of the bacteria was apparent. Since hemolytic *Staph. aureus,* coagulase-positive, had been cultured from the urine, we may assume that this is the same organism. Sections through the myocardium showed many small infarcts which were heavily infiltrated with acute inflammatory cells. Many of these infarcts showed the same bacteria (figure 2), and we assume that these are embolic phenomena. Scattered throughout other areas of the heart was a more diffuse myocarditis, but there was no evidence of an acute myocardial infarct.

The kidneys weighed 240 gm. each. The cortical surfaces were finely granular. There were miliary abscesses throughout the medulla and a few in the cortex. A few papillae were necrotic and covered by a purulent exudate. Microsections of the renal papillae showed not only severe necrosis but also large clumps of coccal bacteria (figure 3). Other sections through the kidney showed severe nephrosclerosis. Microsections of the glomeruli showed the characteristic appearance of intercapillary glomerulosclerosis or Kimmelstiel-Wilson syndrome, with heavy hyalin deposits filling some capillary loops and surrounding many others.

The spleen was large, weighing 320 gm., and contained small infarcts. Microsections of the spleen revealed areas of inflammation and necrosis containing large clumps of coccal bacteria and representing septic infarcts.

The brain also showed septic emboli (figure 4), as Dr. Remenchik predicted.

In summary, the pathologic findings were those of vascular and septic complications of diabetes:

Vascular

Generalized arteriosclerosis

Arteriosclerosis obliterans; leg cramps; skin ulcers; gangrene; amputation

Nephrosclerosis; intercapillary glomerulosclerosis; hypertension; azotemia

Septic

Acute bacterial endocarditis (mitral valve) with rupture; murmurs; fever

Acute necrotizing papillitis; azotemia; fever

Septic emboli and infarcts in myocardium, kidneys, spleen and brain; fever; sepsis; weakness; coma

DR. CALVIN RADIN (staff physician, medical service): What did the liver show?

DR. RUBNITZ: We expect to find some fatty infiltration of the liver in diabetics, but we did not in this case. The liver was of normal size, and only a very few nonspecific focal infiltrates were found.

DR. STANLEY LEITHOLD (attending physician, medical service): I would like to *de*-emphasize the cardiac findings in this case and stress the renal infection. There is no doubt that this patient had endocarditis, but all through his course there was a pyuria. I think it is important to realize that this was *not* primarily an acute endocarditis; rather it was a *renal* infection leading to a septicemia and bacterial endocarditis.

Author's Correction in "Anterior Pituitary Hormones" by Choh Hao Li
POSTGRADUATE MEDICINE, January 1961, pp. 13-23

Figure 1 was reproduced from Li, C. H.: The pituitary. Scient. American 183:19, 1950. Figure 4 was reproduced from Li, C. H. in Neuberger, A.: Symposuim on Protein Structure. London, Methuen & Co., Ltd., 1958, p. 302. The name of the third author in reference 30 should read Buettner-Janusch, V.

Editorials

Postgraduate Medicine

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THE AGING MIND

EVERYBODY knows that people who get really old begin to have trouble remembering. In fact, the favorite medical story of today tells of the elder who came to a psychiatrist and said, "I cannot remember from one minute to the next." "When did this begin?" asked the psychiatrist, and the patient said, "When did what begin?"

The Nuffield Unit for Research Into the Problems of Aging found that the ability to understand something of what is to be remembered decreases with age. The retention of facts is more easily lost in elderly persons, especially if any activity comes between the process of memorizing and the need to recall the fact. Old people have so many memories that they find it difficult to remember new ones. If memories are organized and codified, people remember better. In the British studies, they cited particularly the case of the old person who fills a kettle, puts on the gas, goes to look for matches, and forgets that the gas was turned on. Elderly persons look up a telephone number and, by the time they begin to dial, forget the number.

Short-term memory is essential in many industrial activities. When short-term memory is impaired, the speed and accuracy of making complex movements are greatly lessened. Impairment of short-term memory is especially dangerous in older people who drive cars, since coincidentally comes a delay in their reaction time.

The Nuffield studies show that the touchy temper of aging people has complex causes. "Growing rigidity of habit and outlook can result in an intense distrust of change, especially in those whose lives have run along a confined path. With this is coupled the fear that change will be inevitable when independence decreases—although there is now less fear of poverty there is a terror of becoming institutionalized. The knowledge that almost 90 per cent of the aged in this country manage to live in their own or their relatives' homes helps to reduce the development of this fear. Awareness of failing ability can result in resentment toward offers of help that draw attention to it, or in an access of self-pity when help is not forthcoming. Above all, loneliness and a feeling of being unwanted and, worst of all, not needed, can breed a brooding melancholy."

Dr. Annis Gillie, who opened a discussion

on aging before the Royal Society of Medicine,[1] blames particularly the change in our civilization which has so greatly separated aged persons from the young. "The majority of the young find little pleasure in the society of the aged, and old people are terribly aware of this and sensitive about it. As long as husband and wife are together loneliness is mitigated, and boredom for the woman is rare since she continues to use her domestic skills. The single old person, especially the widower, not only loses daily companionship but the sense of being a part of society as well. For most aging men and women this fear of uselessness and boring isolation is far more insistent than the fear of death, and it is in isolation that mental deterioration most rapidly occurs. However, where the social environment remains good (even if reduced to a society of two) any abrupt change in mental capacity or social behaviour is almost always the result of physical morbidity—a silent coronary attack, a mild cerebral episode, an undiagnosed neoplasm. The family doctor's alertness in discriminating between these two groups is an important factor in the prognosis and rehabilitation of many elderly patients."

Extensive studies have shown that people who have a high level of education or who are skilled craftsmen show the least deterioration in old age, particularly because of the extent of their intellectual and coordinated activities and partly because their work is often independent of any arbitrarily established pace. People of experience learn to economize in both effort and performance. By such automation and by planning in advance, they can conceal diminishing capacity by reducing fatigue and clumsiness. The deliberate exercise of mental reserves leads to storage of memories. Stated more simply, people who continue to use their minds deteriorate less than do those who stop. As great experience is accumulated, the tendency to act and speak quickly develops. Dr. Gillie cited as an example the gift for successful "stop diagnosis," which seems to be the special attribute of some older physicians. At the same time such rigidity of experience may lead to the development of rigid patterns of thought and action.

The depression which sometimes accompanies advancing years is associated especially with compulsory retirement. Dr. T. N. Rudd, Southampton, observed that retirement is for many men the last straw which breaks down an adjustment previously maintained only with difficulty. While good health and intact family relations may support a retiring man for a certain time, he begins almost immediately on retirement to disintegrate. Women do not have this difficulty, since they may continue their task of providing and cooking food and operating the household. Even though an elderly woman's efficiency may decline, the continued performance of her duties preserves her from senile dementia.

Dr. Rudd noted also that old age has ceased to have the respect and honor which was formerly its recognized due. Nowadays, age represents weakness, loss of respect, and tolerance instead of honor. The fear of old age is intolerable in many people and is strongly repressed. The fear is intensified because of a general attitude of disparagement of the aged and the development of prejudice against old age and older people, against parents and parents-in-law, and even against aged persons in hospitals.

Dr. Rudd traced carefully the steps by which the older person progresses to senile dementia: "The loss of his accustomed life satisfactions may come as a sudden blow to the unprepared newly retired individual, and with it the realization that in rejecting old age he is himself being rejected. This can lead to an attitude of self-rejection, a dangerous surrendering to one's environment, rather than the normal healthy pugnacious protection of self-interests. Feelings of guilt at this stage may produce a sense of personal unworthiness. From this the advance into senile dementia can be traced. Self-esteem diminishes, psychological defences crumble, and conscious anxiety and intrapsychic terror develop. Withdrawal, psychotic regression and infantile defence mechanisms now complicate the picture and lead to the familiar state of apathy and disintegration of the personality."

Dr. E. Beresford Davies, Cambridge, observed that old people who live near mental

hospitals are more likely to end in a mental hospital than are those who live some distance from such an institution. In the care of the elderly patients in mental hospitals, electric shock, tranquilizers and psychic energizers have brought about great advancement. Chlorpromazine hydrochloride acts almost specifically to lower tensions and to aid in the disappearance of paranoid ideas. In the hospital the aged have the advantage of the close study of nutrition and metabolism. With proper care, both medical and dietetic, the elderly, depressed and retarded patients may make astounding improvement. The primary measures are the provision of interest and occupation and the associated freedom from both mental and physical pain. The most difficult patients to manage are those who have phobias, anxieties and compulsions and in whom there has been loss of mental control due to the aging process. Then there are elderly people whose minds have failed to such an extent that they are probably better undisturbed, since medical treatment is nothing but the flogging of a dying horse. For such patients, Dr. Davies stated that he prefers tranquilizing and sedative drugs. He especially stressed the need for avoiding overstimulation of the aged. In handicapped and crippled people, rehabilitation has yielded immense successes but there is need for caution in attempts to rehabilitate the exceedingly elderly patient. Dr. Davies believes that for this type of patient music, singing and television are significant in treatment. He concluded his discussion with a statement regarding activity and entertainment: "One of my patients, who was very fond of his pint was urged by me to broaden his interests and even take a little exercise every now and again. To this he replied: 'I appreciate your advice, Doctor. It must be wonderful to know so much about health—but I think you will agree with me that as you look around you will see more old drunkards than old doctors.' "

MORRIS FISHBEIN

REFERENCE

1. Gillie, A., Rudd, T. N. and Davies, E. B.: Discussion of the aging mind. Proc. Roy. Soc. Med. 53: 131-135 (February) 1960.

ARTHROPOD-BORNE VIRUSES

During 1959, the Rockefeller Foundation appropriated $1,194,640 in support of virus research. This was about $150,000 more than was appropriated in 1958. The Foundation maintains laboratories in New York, South America, South Africa, India and California. Already research has shown that there are close relationships between the arthropod-borne viruses, for example, between the virus causing St. Louis encephalitis in the United States and that causing Japanese B encephalitis. A virus known to cause encephalitis in sheep in Scotland was found to be closely related to the virus which causes Russian spring-summer encephalitis. The viruses of yellow fever and dengue are also allied.

Whereas some 20 diseases were known to be caused by viruses 20 years ago, the number today is somewhere between 50 and 60. Twenty-seven agents known or suspected of being borne by arthropods have been described. One hundred and ten probably distinct agents are under consideration. More than 50 distinct agents have been isolated from the blood of patients with febrile illnesses. In his annual report, the president of the Rockefeller Foundation has made an extensive review of this great contribution to the advancement of medical science.

In the Temperate Zone explanations are being sought as to how the arthropod-borne viruses are maintained during cold months, when the insect vectors are scarce. The ticks have a long life and can carry infection over from one season to the next. For the mosquito-borne agents, the hypothesis is that an infected hibernating mosquito is the link between seasons. Infected birds are also assumed to carry viruses over from one season to the next. Indeed, the various forms of equine encephalitis are probably carried by migrating birds. Since some investigators doubt these beliefs, other possible mechanisms involving small rodents, bats, snakes or hedgehogs are also being investigated.

This field of investigation may not at this time be close to the problems of disease in the United States, but, with the present con-

ditions of communication around the world, the physician must be constantly aware and suspicious of these possibilities.

MORRIS FISHBEIN

ANIMAL EXPERIMENTATION

To the current Congress will come a peculiar proposal for legislation to control animal experimentation. The procedures involved would make animal experimentation not only difficult but indeed impossible. As a part of its public relations program to meet this attack, the National Society for Medical Research is asking for nominations for the Research Dog Hero of 1960.

In the past, this designation has been given to other dog heroes, including Annie Okra (Marquette University School of Medicine), used in experiments to develop a blood plasma substitute from okra; Susie (Albany Medical College of Union University), a dog with plastic heart valves; Stinky (Indiana University School of Medicine), the first dog to recover from spinal cord surgery; Airplane (Harvard Medical School), used in experiments to develop plastic patches for special defects; Big Ben (Tulane University School of Medicine), used in research to prove the technic of localized perfusion with anticancer drugs; and Ruff (Maimonides Hospital, San Francisco), now living happily with a second "booster" heart refashioned from part of his diaphragm, a muscular aid which someday may mean the difference between life and death for some 500,000 Americans with heart disease.

I have been wondering whether or not this type of an appeal will really be helpful. Is an emotional appeal in these circumstances better than strict scientific reasoning?

MORRIS FISHBEIN

THE COFFEE BREAK

According to Dr. W. A. R. Thomson, writing in the *Practitioner*, London, eight billion cups of coffee are consumed annually in the United States. On a typical winter day, 24 million persons have a coffee break. Someone has estimated that these rest periods cost the employer 5.5 cents per employee per hour. These statistics are taken from an article by Professor Jean Felton which appeared in *Industrial Medicine and Surgery*. Recently, an employer who was somewhat disturbed by some misdemeanors on the part of his secretary gave her what is commonly called a "bawling out." She responded, "I would just like to change places with you sometime so that you could see what my responsibilities are." He answered, "I would like to change places with you, but I just couldn't drink that much coffee."

Professor Felton insists that there is no real evidence that the coffee break "increases production, improves morale, minimizes absenteeism, lowers labor turnover, drops the accident frequency rate, or eliminates fatigue." She does not believe the statistics. She says instead that the greatest benefit is in the form of better interpersonal relations among workers, brought about by getting together twice a day over a cup of coffee. This goes a little beyond what happens in most places, since employees in general drink their coffee in isolation, particularly in modern plants where the coffee is served to employees at the desk or bench in order to eliminate excessive loss of time. Professor Felton believes the coffee break is a mechanism for relieving tensions and for supporting weakened egos.

Some kind of controlled research still needs to be done to determine just exactly what the values are. Until such research is done, I myself will continue to have coffee breaks because I like coffee.

MORRIS FISHBEIN

EDITORS' NOTE

Our attention has been directed to a supplementary bibliographic reference (J. Am. Dent. A. 55:873, 1957) which challenges certain statements made in reference No. 19 of the bibliography included with the article, "The safety of fluoridation," by Dr. James H. Shaw, published in the December 1960 issue of this Journal.

in any urinary tract infection: "it is the kidney which is the most important consideration"[1]... "Infections limited to the lower urinary tract are comparatively rare"[2]

In the bloodstream, free FURADANTIN and FURADANTIN bound to plasma proteins are in equilibrium ⇌ Free FURADANTIN passes readily through the glomerular filter. Protein-bound FURADANTIN, however, is not filtered by the glomerulus and reaches the peritubular capillaries. Here equilibrium is restored, and the FURADANTIN released from its bound state diffuses through the interstitial spaces and is secreted by the tubular cells. Exacting studies "suggest a three-component system for the renal transport of nitrofurantoin. That is, this nitrofuran appears to be filtered at the glomeruli and both secreted and reabsorbed by the tubules."[3]

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SUPPLIED: Tablets, 50 and 100 mg.; Oral Suspension, 25 mg. per 5 cc. tsp.

*Conservative estimate based on clinical use since introduction.

REFERENCES: 1. Thompson, I. M.: Family Physician, Chicago 9:14, 1959. 2. Campbell, M. F.: Mod. Med. 24:85, 1956. 3. Paul, M. F., et al.: Am. J. Physiol. 197:580, 1959. 4. Johnson, S. H., III, and Marshall, M., Jr.: J. Urol., Balt. 82:162, 1959. 5. Lippman, R. W., et al.: J. Urol., Balt. 80:77, 1958.

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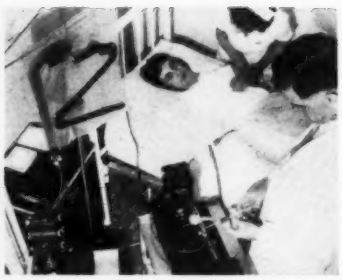


• PERFUSO-PAC

DESCRIPTION: Certain cancers and massive infections can be treated through regional perfusion with this disposable plastic device (upper left). The Perfuso-Pac permits localized treatment with huge doses of medications that could not be used in such quantities if they were allowed to enter the general blood circulation.
PRODUCER: Baxter Laboratories, Inc., Morton Grove, Ill.

• MSC TRIAMINIC®

PURPOSE: Decongestive, antihistaminic and antisecretory therapy.
COMPOSITION: Each timed-release tablet contains:

Phenylpropanolamine hydrochloride	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.
Methscopolamine nitrate	4 mg.

HOW SUPPLIED: Bottles of 50.
PRODUCER: Dorsey Laboratories, a division of The Wander Company, Lincoln, Nebr.

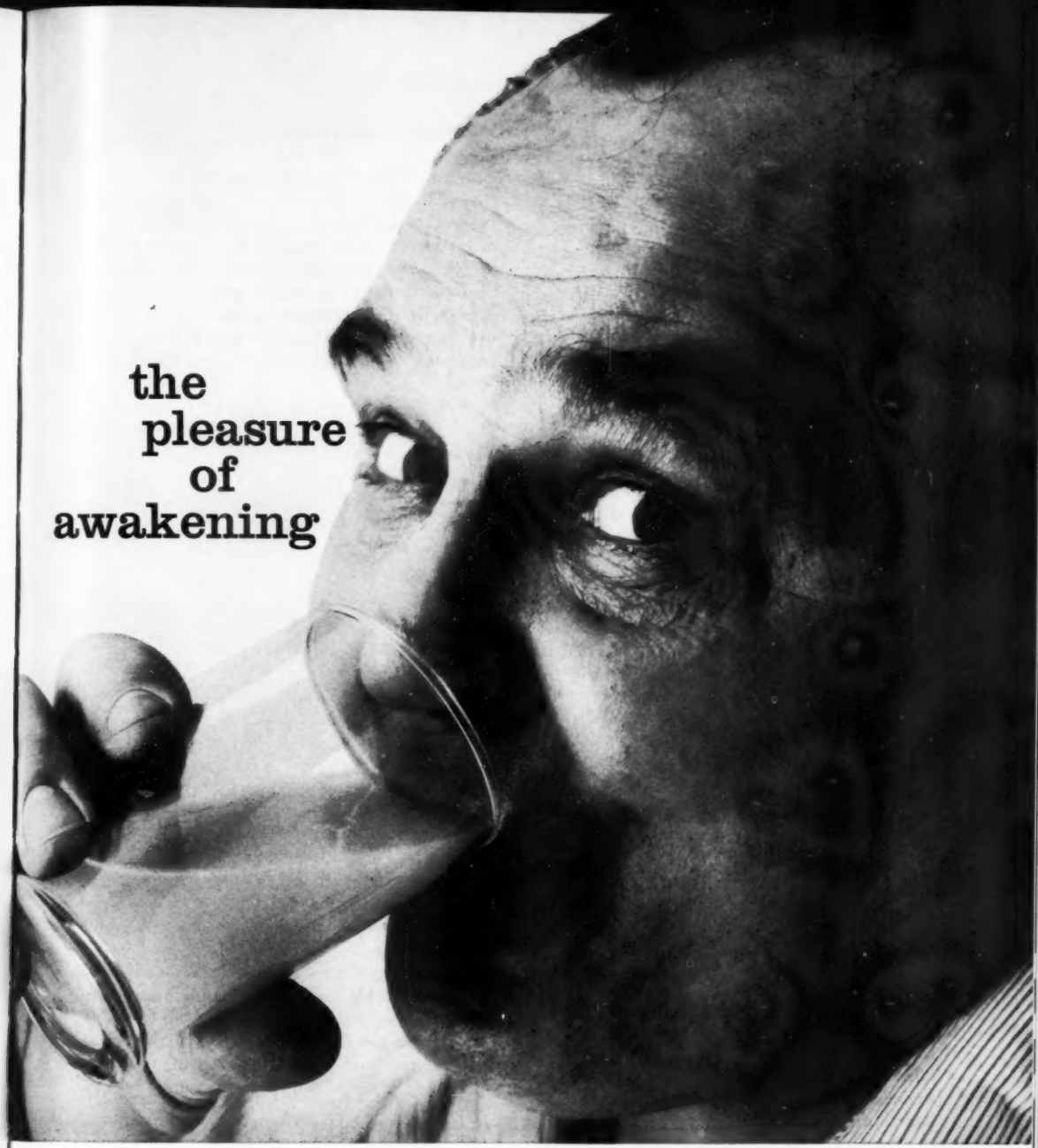
• TAO® READY-MIXED ORAL SUSPENSION
(New Product Form)

PURPOSE: Medium-spectrum antibiotic therapy.
COMPOSITION: Triacetyloleandomycin.
CAUTION: Mild, reversible jaundice has been observed in pediatric patients when more than the recommended dosage of this preparation has been administered.
DOSAGE AND ADMINISTRATION: For adults, from 250 to 500 mg. four times daily, depending on severity of infection. The usual pediatric dosage is 3 to 5 mg. per pound of body weight every six hours.
HOW SUPPLIED: 60 cc. bottles.
PRODUCER: J. B. Roerig and Company, Division of Chas. Pfizer & Co., Inc., New York.

• SURGICEL

DESCRIPTION: Used to control bleeding in both external and internal wounds, this dressing is an oxidized, regenerated cellulose. It induces an artificial clot within two to three minutes after contact with the wound, and can be left in the wound; it is readily absorbed by the tissues and disappears completely, usually within two weeks. Applied in gauzelike strips or carded fiber pads, the dressing can be used to stem hemorrhage in operative procedures on the heart, liver, spleen and other parts of the body in which bleeding is difficult to handle, and in dental extractions involving hemophiliacs.
PRODUCER: Johnson & Johnson, New Brunswick, N. J.

(Continued on page A-116)



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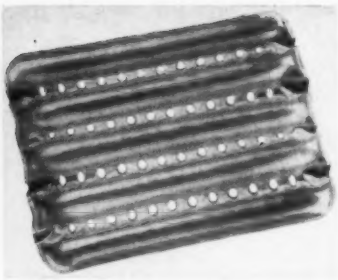

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DESCRIPTION: Constructed of vinyl plastic, this sanitary cushion of low-pressure air eliminates pressure points on the body. It will not absorb odors, is easily washed and disinfected, and, if punctured, can be repaired with plastic cement. Extremely cool because of the ventilation holes and channels between tubes, this cushion will not mat or pack down from perspiration or other moisture. It measures 15½ by 17½ in. and weighs 7 oz.; when deflated, it can be carried in a pocket or small purse. A separate tube for inflation is available.
PRODUCER: Howard Sales Co., Pasadena, Calif.

• ZARONTIN®

PURPOSE: To treat petit mal epilepsy.
COMPOSITION: Each capsule contains 0.25 gm. ethosuximide.
HOW SUPPLIED: Bottles of 100.
PRODUCER: Parke, Davis & Company, Detroit.

• CALCIDRINE® SYRUP

PURPOSE: To treat coughs due to colds.
COMPOSITION: Each fluid ounce contains:

Codeine phosphate	64.8 mg.
NEMBUTAL® sodium	25 mg.
Ephedrine hydrochloride	25 mg.
Anhydrous calcium iodide	910 mg.

CAUTION: This syrup should not be given to persons with thyroid disease or an allergic sensitivity to iodides.
DOSAGE AND ADMINISTRATION: For adults, 1 to 2 teaspoonfuls every two to four hours; for children 6 to 10 years old, 1 teaspoonful; for children less than six years old, as directed by the physician.
HOW SUPPLIED: 4 fl. oz., 1 pt. and 1 gal. bottles.
PRODUCER: Abbott Laboratories, North Chicago.

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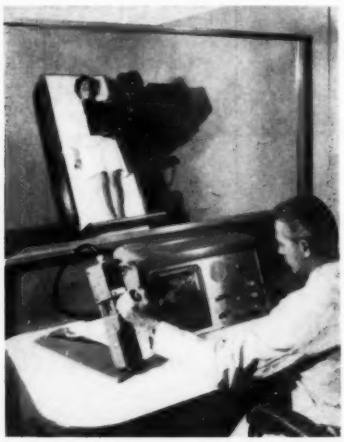
PURPOSE: Prevention and treatment of iron-deficiency anemia.
COMPOSITION: Each Chronosule contains 6 mg. molybdenum oxide and 390 mg. ferrous sulfate.
DOSAGE AND ADMINISTRATION: For adults, 1 Chronosule daily; in severe anemia, 2 Chronosules daily. For children, 1 Chronosule daily.
HOW SUPPLIED: Bottles of 30 and 250.
PRODUCER: White Laboratories, Inc., Kenilworth, N. J.



• SATELLITE

DESCRIPTION: Procedures formerly possible only at close range may be performed by remote control with this television x-ray system. The unit includes a remote-control x-ray table and image amplifier. The remote controls are identical to those on the table itself, and all equipment movements are motor-driven. If desired, the remote-control unit can be set up behind a protective screen in the same room with the patient.
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• BETADINE® SWAB AIDS

DESCRIPTION: Packed in a dispenser box designed for wall mounting, these disposable antiseptic applicators are individually wrapped in cellophane tear-off envelopes. Each swab contains povidone-iodine N.N.D.
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(Continued on page A-119)

• **ANAMEBA®**

PURPOSE: To treat amebiasis.
COMPOSITION: Each tablet contains 5000 U.S.P. units of bacitracin methylenedisalicylate and 125 mg. iodochlorhydroxyquin.
DOSAGE AND ADMINISTRATION: 1 tablet three times a day for eight days.
HOW SUPPLIED: Bottles of 24.
PRODUCER: Chicago Pharmacal Co., Chicago.

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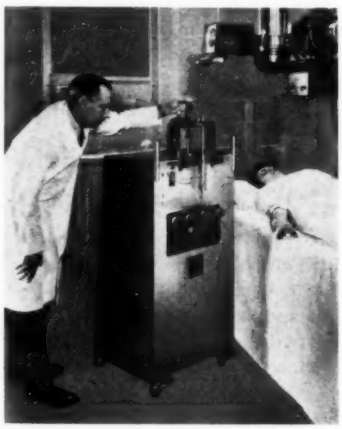
PURPOSE: To restore or maintain proper metabolic balance.
COMPOSITION: Oxymetholone.
HOW SUPPLIED: 10 mg. tablets in bottles of 30.
PRODUCER: Parke, Davis & Company, Detroit.



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DESCRIPTION: For use in circulatory studies, this high-pressure injector discharges warmed, undiluted radiopaque fluid into the blood stream in a single burst. Pressure (75 to 1,075 lb. per square inch), injection speed and quantity of fluid are preselected. In one second the unit can inject up to 34 cc. of 90 per cent HYPAQUE® or equivalent medium fluid heated to 40° C. The stainless steel, 60 cc. capacity syringe is loaded automatically; a purging system removes air bubbles. The unit operates on 110 V, 60 cycle AC current. Pressure is generated by torque springs, and a single switch coordinates injection, x-ray exposure and film transport by remote control. An optional twin mount and extra syringe, each offering 537 lb. of pressure, adapt the unit to bilateral angiography.
PRODUCER: Picker X-Ray Corporation, White Plains, N. Y.

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DESCRIPTION: An electronic direct-writing device for recording pupillary movement, this instrument measures absolute pupil size and follows oscillations in a pupillary diameter measuring 0.025 mm. or less. The unit has a stability error of ± 0.5 per cent over long periods.
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Phenylephrine hydrochloride	30 mg.
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Sodium citrate	1.2 mg.
Decapryn (doxylamine) succinate	36 mg.

These agents are combined in an aromatized syrup containing thyme, tolu and menthol.
CAUTION: May be habit-forming.
DOSAGE AND ADMINISTRATION: The following doses are to be administered every three to five hours: for adults, 1 teaspoonful, not to exceed 6 teaspoonfuls in 24 hours; for children 6 to 12 years old, ½ teaspoonful, not to exceed 3 teaspoonfuls in 24 hours.
HOW SUPPLIED: 1 pt. and 1 gal. bottles.
PRODUCER: The Wm. S. Merrell Co., Cincinnati.

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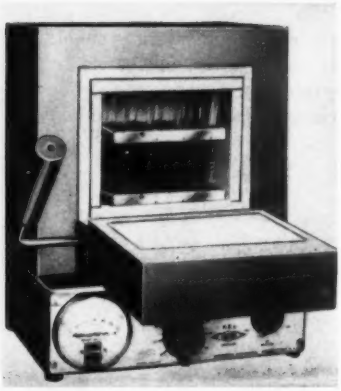

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HOW SUPPLIED: Bottles of 30 and 100.
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• BUCALAMASE®

DESCRIPTION: A buccal form of alpha amylase, this agent relieves pain and inflammation in orthopedic conditions. It is available in tablets.
PRODUCER: Rystan Company, Mount Vernon, N. Y.

• COSA®-TERRASTATIN CAPSULES AND ORAL SUSPENSION

PURPOSE: Antibiotic and antifungous therapy.
COMPOSITION: Each capsule contains:

TERRAMYCIN®	250 mg.
Glucosamine hydrochloride	250 mg.
Nystatin	250,000 units

Each 5 cc. of the oral suspension contains the above ingredients in one-half the amounts listed.
DOSAGE AND ADMINISTRATION: For adults, 1 to 2 gm. daily in divided doses; for children, 10 to 20 mg. per pound of body weight daily in divided doses.
HOW SUPPLIED: Capsules: bottles of 50; suspension: 2 oz. bottles.
PRODUCER: Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., Brooklyn.

• DEBAKEY-COOLEY LONG FORCEPS

DESCRIPTION: Made of Swedish stainless steel, this hand-finished instrument is designed for thoracic, cardiovascular, deep abdominal and gallbladder surgery. It is available in 7¼, 9, 10 and 11 in. lengths and weighs approximately one-half as much as forceps presently available for deep dissecting. Special features are a one-and-four nonslip ratchet incorporated in the handle and fine points designed for manual precision. Both curved and right-angled models of the forceps are available.
PRODUCER: Dennis R. Scanlan, Inc., St. Paul.

• CLINICAL TEST KITS

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PRODUCER: Omni-Tech, Inc., Sun Valley, Calif.

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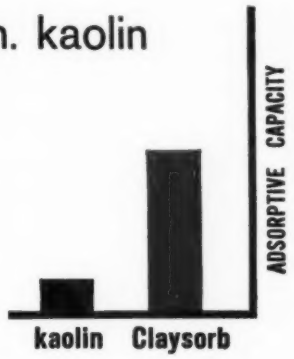

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► COMPLICATIONS IN SURGERY AND THEIR MANAGEMENT

Edited by Curtis P. Artz, M.D., Associate Professor of Surgery, and James D. Hardy, M.D., Professor and Chairman, Department of Surgery, University of Mississippi School of Medicine, Jackson, with 71 contributors. 1,075 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $23.00.

Most surgical textbooks are concerned only with indications for surgery and proper technics. Until this book was published, the complications of surgery regrettably had received inadequate coverage. With the objective of producing a single volume covering surgical complications, the editors chose contributors who are well known for their original contributions to surgery.

The complications discussed include those that may occur in any surgical patient (wound infection, hemorrhage, shock and conditions resulting from administration of transfusions, antibiotics and parenteral fluid) and those involving organs and systems (renal and liver failure, involvement of the cardiorespiratory system, and venous thromboses). A separate section deals with complications of anesthesia, radiation therapy, nutritional problems and psychologic factors in the postoperative period.

The greater part of this book is devoted to a systematic review of the various operative procedures, discussed according to organs, systems or regional anatomy. Indications for surgery are not considered in detail, but all the common and most of the unusual complications are discussed in terms of etiology, prevention, diagnosis, treatment and prognosis. The completeness of the various presentations is impressive.

Particularly useful are the illustrations and discussions of those steps in operative procedures in which errors in technic are likely to give rise to complications. Equally important are the discussions on the recognition and correction of errors made before complications arise.

Y. S.

► THE YEAR BOOK OF PEDIATRICS (1960-1961)

Edited by Sydney S. Gellis, M.D., Professor and Chairman, Department of Pediatrics, Boston University School of Medicine, Boston. 479 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $8.00.

The current volume of this annual series contains reviews of world pediatric literature for the year prior to September 1960 in concise, readable abstracts. The material is divided as it applies to the various organ systems or subgroups of pediatric interest. As usual, the comments of the editor furnish some of the most interesting reading in the book, and at times his sense of humor proves his point admirably. The illustrations are of good quality and enliven the text.

This book contains the meat of the progress which has been made in pediatrics since the last Year Book in this field was published. It is a volume to which one easily becomes addicted by frequent use and referral in a busy practice.

S. D. M.

(Continued on page A-148)

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1. Critchley, M.: **British, M. J.**, 2:1214 (Nov. 15) 1958.
2. England, A. C., and Schwab, R. S.: **A.M.A. Arch. Int. Med.** 104:439 (Sept.) 1959.
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► MODERN OCCUPATIONAL MEDICINE

Edited by A. J. Fleming, M.D., Medical Director, C. A. D'Alonzo, M.D., Assistant Medical Director, Medical Division, and J. A. Zapp, Ph.D., Director, Haskell Laboratory for Toxicology and Industrial Medicine, E. I. Du Pont de Nemours & Company, with 22 contributors. Ed. 2. 586 pages with 66 illustrations and one color plate. 1960, Lea & Febiger, Philadelphia. $12.00.

All the contributors to the thoroughly revised second edition of this volume are associated in some capacity with E. I. Du Pont de Nemours & Company, and all are specialists in their fields. This book has been developed with the idea of presenting valuable information resulting from their many years of experience.

Basically, modern occupational medicine is preventive medicine. Nothing pertinent in this field seems to have been omitted from this book. Subjects range from the evaluation of medical services in industry to biostatistics in occupational medicine.

The material presented should prove useful to physicians, executives, safety engineers and chemists in industry as well as to physicians who treat occupational diseases in private practice.

I. P. F.

► AN ATLAS OF NEUROSURGICAL TECHNIQUES

By James L. Poppen, M.D., Neurosurgeon, Lahey Clinic, Boston. 522 pages, illustrated. 1960, W. B. Saunders Company, Philadelphia and London. $28.00.

Written by Dr. Poppen of the Lahey Clinic and ably illustrated by P. D. Malone, Robert Ullrich, Melford D. Diedrick and Francis E. Steckel, this atlas is an excellent text of neurosurgical procedures.

Sections of the text cover the procedures involving the scalp, skull and intracranial contents and illustrate the treatment of both intracranial and extracranial lesions of the cranial nerves. The author has summarized the treatment of trigeminal neuralgia, from local injections of alcohol and avulsions of peripheral nerves to intracranial procedures for section of the fifth cranial nerve. Surgical management of peripheral nerves is discussed and the surgical treatment of various intraspinal lesions is illustrated.

The section on the treatment of intracranial aneurysms and vascular anomalies of the brain is a valuable addition to the book. The illustrations of the various locations of intracranial aneurysms in both the carotid circulation and the vertebral and basilar circulation are an excellent review, and Dr. Poppen's skill in treating these vascular lesions is well known.

R. H. M.

► CLINICAL VECTORCARDIOGRAPHY AND ELECTROCARDIOGRAPHY

By Edward Massie, M.D., Associate Professor of Clinical Medicine, and Thomas J. Walsh, M.D., Instructor of Clinical Medicine, Washington University School of Medicine, St. Louis. 592 pages, illustrated. 1960, The Year Book Publishers, Inc., Chicago. $27.50.

A workbook as well as a textbook, this volume is one of an increasing number of publications in this field, evidencing a growing interest in a new diagnostic discipline. Although simplicity and directness are the basic aims in this text, anyone who masters its contents will have more than a superficial acquaintance with the subject.

The first two sections of the book present the body of the material designed to relate electrocardiography with vector interpretation of conventional electrocardiograms and spatial vectorcardiography. An adequate discussion follows on the cardiac arrhythmias and other conditions. An additional section contains a bibliography, an index and many excellent reproductions of vectorcardiograms and electrocardiograms.

A large amount of information is provided in this book; however, the attempt at completeness is one of its weaknesses.

The bibliography is less accessible in the appendix than it would have been at the end of each chapter.

These criticisms do not seriously impair the value of this book. The material is presented clearly, and the basic concepts are explained in greater detail than in many books for beginners in this field. If previous attempts to learn about vectorcardiography have been unrewarding, this volume should prove to be useful.

J. A. C.

(Continued on page A-150)

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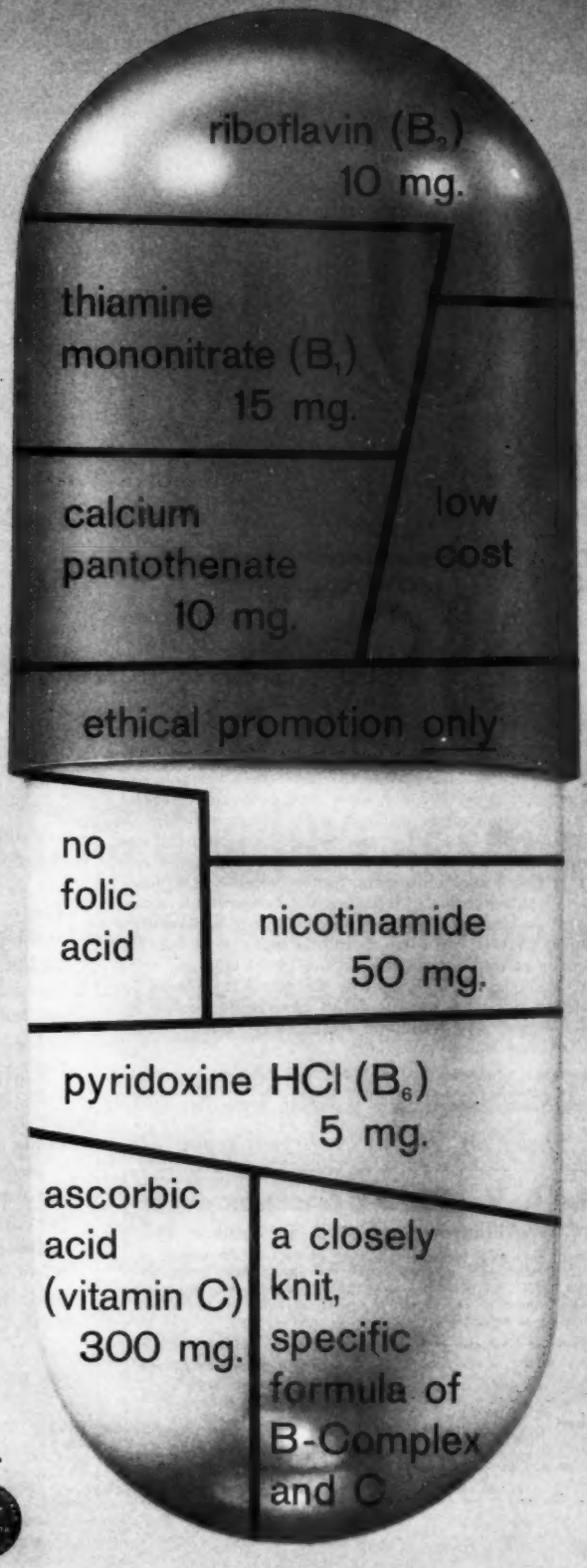
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► ORAL PATHOLOGY

By Kurt H. Thoma, D.M.D., Professor of Oral Surgery, and Henry M. Goldman, D.M.D., Professor and Chairman, Department of Stomatology, Boston University School of Medicine, Boston. Ed. 5. 1,523 pages with 1,704 illustrations, 111 in color. 1960, The C. V. Mosby Company, St. Louis. $27.50.

Through the years this book has been a favored reference and a standard text. Its fifth edition is enhanced by the coauthorship of Dr. Henry M. Goldman, who has contributed much to the knowledge and understanding of diseases affecting the head, neck and jaws.

Many specialists will find this text of value. For example, the discussion on developmental anomalies in teeth will be of great interest to the pediatrician and all medical specialists, since the calcification of the teeth forms a permanent record of a patient's medical history and makes it possible to ascertain time of onset of disease disturbances up to age 20.

Changes in the form and structure of the teeth and the relation between these disturbances and systemic diseases are thoroughly discussed. Some systemic diseases, especially those of the endocrine system, affect the tooth-supporting structures; these relations are well covered and are illustrated by case reports, photographs and roentgenograms, providing a basic understanding of the dental manifestations in each instance. The connection between diabetes and infection in the periodontium and the effect of scleroderma on the periodontal membrane and of hyperparathyroidism on the lamina dura of the tooth socket are but a few of the disorders discussed.

Localized dental diseases and their complications are presented. Dental caries, pathologic findings in the pulp, root-end infections, periodontal disease, and bacterial infections of bone and soft tissue are described in detail.

Several chapters are devoted to developmental, acquired and congenital defects of the head and jaw, and many case reports are included. One chapter is devoted to treatment of disorders that affect the temporomandibular joint; another deals with neurologic and other facial pain entities. Cysts and tumors of the hard and soft tissue of the head and neck and metastatic tumors are thoroughly discussed.

R. J. G.

(Continued on page A-152)

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► BLOOD DISEASES OF INFANCY AND CHILDHOOD

By Carl H. Smith, M.D., Professor of Clinical Pediatrics, Cornell University Medical College, New York. 572 pages, illustrated. 1960, The C. V. Mosby Company, St. Louis. $17.00.

Presenting "the essentials of pediatric hematology in concise form against the background of normal development in infancy and childhood," this volume fills a long-felt need in pediatric publications. Included in the text are discussions of the origin of blood cells, the changes in the blood during infancy and childhood, and the genetic origin and transmission of blood disorders in the early years of life. Attention is given to the blood groups in relation to transfusions in pediatric practice and the differential diagnosis of jaundice in newborns. Erythroblastosis foetalis is discussed extensively, and the anemias are categorized and dealt with individually. Disorders of leukocytes, the spleen and reticuloendothelial system, blood clotting and the purpuras are considered. Newer developments in the field of immunohematology and in the rapidly increasing list of inborn errors of metabolism also are presented.

This book is not intended to supplant the standard hematologic texts but to cover in one volume the disorders of the blood that are seen in childhood and to emphasize the pathogenesis of hematologic disorders as a basis for treatment by established concepts. The emphasis is on practicality, so that the medical practitioner, by careful history taking and physical examination and use of simple instruments and technics, might manage successfully the common blood disorders of children.

S. D. M.

► FUNDAMENTALS OF CHEST ROENTGENOLOGY

By Benjamin Felson, M.D., Professor and Director, Department of Radiology, University of Cincinnati College of Medicine, Cincinnati. 301 pages with 450 illustrations. 1960, W. B. Saunders Company, Philadelphia and London. $10.00.

The mutual dependence of surgery and radiology is illustrated particularly well in pulmonary disease. Chest films, bronchograms and laminagrams have been available to physicians for many decades; however, only with the increasing ability of surgeons to treat lesions formerly considered inoperable has there come the new and intensified interest in pulmonary radiology which is so well expounded in this book.

Dr. Felson is a leader in this field. His refresher courses at national meetings are "sellouts," and his new book should prove both popular and useful.

Particularly excellent are the 75 well-illustrated pages of the chapters on the lobes and the segments. I would have been happier had the 13 pages on chest fluoroscopy been replaced by the simple statement that this procedure, although helpful, is not essential and, because of its danger to patients and physicians, should be abandoned. Furthermore, I marvel that Dr. Felson, like so many other competent radiologists, is willing to spend so much time and effort deducing the spatial relationships of structures seen in nonstereoscopic chest films when stereoscopy would settle the matter promptly and easily.

These trivia, however, do not mar the excellence of a timely, authoritative and helpful piece of medical writing.

P. C. H.

► CARCINOMA IN SITU OF THE UTERINE CERVIX

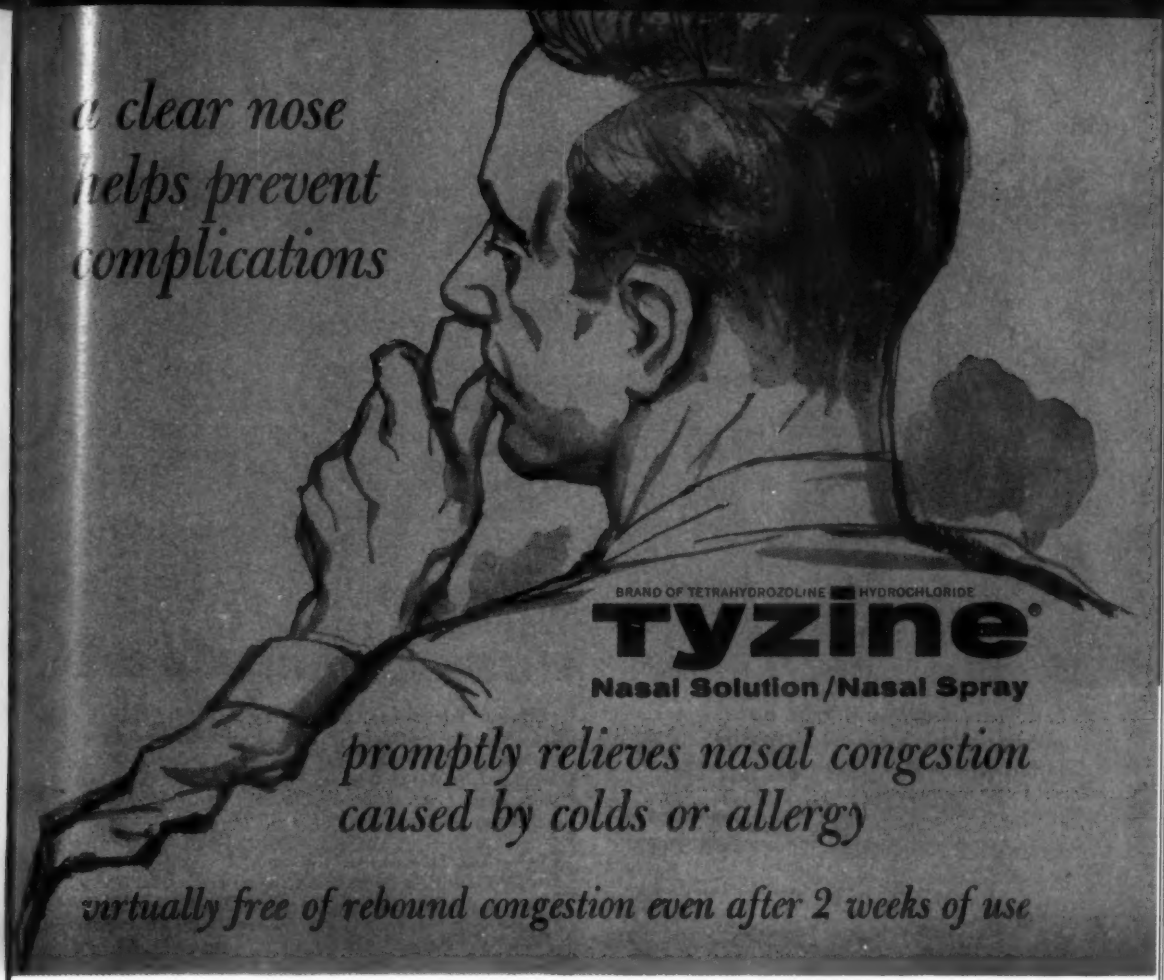
By Gilbert H. Friedell, M.D., Associate Pathologist, Massachusetts Memorial Hospitals, Arthur T. Hertig, M.D., Head, Department of Pathology, and Paul A. Younge, M.D., Assistant Clinical Professor of Gynecology, Harvard Medical School, Boston. 154 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $7.50.

From a minimal number of cases the authors have drawn their conclusions on the manner of diagnosis and the principal forms of treatment of carcinoma *in situ* of the uterine cervix. Excellent photomicrographs document their work. At the conclusion of this monograph an illustrative discussion of Schiller's test is provided.

As stated by the authors, the problem of carcinoma *in situ* is a complex one in diagnosis and management, and the histologic interpretation and treatment can be based only on wide experience and wisdom.

E. A. B.

(Continued on page A-154)



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► DIABETES

By Robert H. Williams, M.D., Executive Officer and Professor of Medicine, University of Washington School of Medicine, Seattle, with 54 contributors. 793 pages with 192 illustrations. 1960, Paul B. Hoeber, Inc., Medical Book Division of Harper & Brothers, New York. $20.00.

One of the finest books on diabetes mellitus, this volume covers all aspects of the disease. A large portion of the text is devoted to the clinical aspects of diabetes, including etiology, pathology, diagnosis, treatment, complications and prognosis, as well as diabetic acidosis, the use of oral hypoglycemic agents, and diabetes in childhood and during pregnancy. The remainder of the book covers more basic subjects such as the chemistry of insulin, its secretion and distribution in the body, and methods used for the assay of insulin in the plasma. The relationship of glucagon, adrenal steroids and growth hormone to diabetes also is considered. Insulin antagonism, plasma lipids, alpha-cell cytotoxins, hypoglycemosis, experimental diabetes and numerous other subjects are discussed.

The text is well written and well illustrated, and a good bibliography follows each chapter.

R. V. R.

Books received are acknowledged in this department. As space permits, books of principal interest to our readers will be reviewed more extensively. Additional listings will be found on pages 261, 308 and 313 of this issue.

Hormones in Human Plasma; Nature and Transport. Edited by Harry N. Antoniades, Ph.D., Protein Foundation Laboratories, Jamaica Plain, Massachusetts, with 33 contributors. 667 pages, illustrated. 1960, Little, Brown & Company, Boston. $25.00.

Annals of the New York Academy of Sciences, 1960. Biochemical Aspects of Microbial Pathogenicity. Vol. 88, Art. 5. 297 pages, illustrated. $5.00.

Light Coagulation. By Gerd Meyer-Schwickerath, M.D., Professor of Ophthalmology, Rheinische Friedrich-Wilhelms-Universitat Medizinische Fakultat, Bonn, West Germany. 114 pages with 55 figures, including seven in color. 1960, The C. V. Mosby Company, St. Louis. $9.50.

The Cutaneous Manifestations of the Benign Inflammatory Reticuloses. American Lecture Series. Edited by Samuel M. Bluefarb, M.D., Associate Professor of Dermatology, Northwestern University Medical School, Chicago, with three contributors. 408 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $14.00.

Healthy Babies—Happy Parents. By Henry K. Silver, M.D., Professor of Pediatrics, C. Henry Kempe, M.D., Professor and Chairman, Department of Pediatrics, University of Colorado School of Medicine, and Ruth Svibergson Kempe, M.D., Denver. 228 pages, illustrated. 1960, The Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto and London. $4.50.

Bleeding Syndromes; a Clinical Manual. American Lecture Series. By Oscar D. Ratnoff, M.D., Associate Professor of Medicine, Western Reserve University School of Medicine, Cleveland. 287 pages. 1960, Charles C Thomas, Springfield, Illinois. $8.50.

Pathology; a Dynamic Introduction to Medicine and Surgery. By Thomas Martin Peery, M.D., Professor of Pathology, and Frank Nelson Miller, Jr., M.D., Associate Professor of Pathology, George Washington University School of Medicine, Washington, D. C. 626 pages. 1961, Little, Brown & Company, Boston. $5.50.

The Transplantation of Tissues and Organs. By Michael F. A. Woodruff, M.D., Professor of Surgical Science, University of Edinburgh Faculty of Medicine, Edinburgh, Scotland. 777 pages, illustrated. 1960, Charles C Thomas, Springfield, Illinois. $25.50.

Clinical Toxicology. By C. J. Polson, M.D., Professor of Forensic Medicine, University of Leeds School of Medicine, and R. N. Tattersall, M.D., Assistant Physician to the Leeds General Infirmary, Leeds, England. 589 pages. 1961, J. B. Lippincott Company, Philadelphia and Montreal. $10.00.

Infectious Diseases of Children. By Saul Krugman, M.D., Professor and Chairman, Department of Pediatrics, New York University School of Medicine, New York, and Robert Ward, M.D., Professor and Head, Department of Pediatrics, University of Southern California School of Medicine, Los Angeles. Ed. 2. 398 pages with 55 illustrations and seven color plates. 1960, The C. V. Mosby Company, St. Louis. $13.00.

Cell Physiology of Neoplasia. Collection of papers presented at the Fourteenth Annual Symposium on Fundamental Cancer Research, 1960. Edited by the Publications Department of The University of Texas M. D. Anderson Hospital and Tumor Institute, Houston. 653 pages, illustrated. 1961, University of Texas Press, Austin. $10.50.

Heart Sounds and Murmurs; a Clinical and Phonocardiographic Study. By P. A. Ongley, M.D., Consultant in Pediatrics, Mayo Clinic, Rochester, Minnesota, Howard B. Sprague, M.D., Board of Consultation, Massachusetts General Hospital, Boston, M. B. Rappaport, E.E., late Head of Department of Electrophysiologic Research, Sanborn Company, Waltham, Massachusetts, and A. S. Nadas, M.D., Cardiologist, Children's Hospital, Boston. 360 pages with 211 illustrations. 1960, Grune & Stratton, Inc., New York and London. $9.75.

Surgical Diseases of the Chest. Edited by Brian Blades, M.D., Professor of Surgery, George Washington University School of Medicine, Washington, D.C., with 18 contributors. 580 pages with 267 illustrations. 1961, The C. V. Mosby Company, St. Louis. $22.00.

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DR. Pepys' Pages

Personal Diary
and Observations on
Medical Life
by MORRIS FISHBEIN, M.D.

Jan. 1—Recovering from the excesses of the previous evening, and in the afternoon to play games with Samuel Mantel, William P. Meyers and Carroll Kahn.

Jan. 2—In the morning reading a mystery, "The Progress of a Crime," by Julian Symons—tops in detection. In the evening by plane back to Chicago, arriving just in time to see the final few minutes of the Rose Bowl game. Then to dine with the Rooneys, the Russos, Dr. Daro and others, celebrating the twenty-fifth anniversary of the François Popes.

Jan. 3—At noon with the great Mortimer, who has built the Northwest Highway and other roads, Bill Hoffman, Morris Friedell, and Novak to form a research foundation. In the evening to a temple to speak on the works of Maimonides.

Jan. 4—With Amy Louise and Danny to appear on Don McNeill's Breakfast Club. At noon to the meeting of the Public Education and Heart Service Council of the Chicago Heart Association, hearing of the new programs developed by Kelly, Kate Cohn, Jones, Oberlander and others; Mark Lepper presided most efficiently and great progress was made.

Jan. 5—All this day at the desk. In the evening to hear the great Pierre Monteux, now 86 years old, lead the Chicago orchestra in amazing performances of the works of Stravinsky and Cesar Franck.

Jan. 6—All this day at the desk, reading also the novel "I Swear and Vow," by Dr. Stefan Olivier, which concerns a hospital in West Germany.

Jan. 7—The editorials for a variety of publications and the scripts for various articles involve a mass of reading. This day, lightened the time with paperbacks of mayhem, murder and lust, and glad to go early to bed.

Jan. 8—In the afternoon to dine with Justin and Ann at Fritzel's, and then to sit for wellnigh four hours watching the motion picture "Exodus." The color photography of Cyprus and Israel is superb.

Jan. 9—After disposing of the correspondence, spent two hours making a tape recording for a Norman Ross show dealing with the book "Heart Care." Also participating were Willis Potts, De Takats, Norman Roberg, Pete Talso and Lev, and the conversation was beautifully moderated by Norman Ross.

Jan. 10—By early jet to New York in one hour and 30 minutes; then to a conference at Doubleday's on the progress of my various works. In the evening came Milton and Sylvia Lasdon to dine with us at the Marco Polo Club, and thereafter to see Lucille Ball perform with vim, vigor, and vitality in "Wildcat."

Jan. 11—To breakfast came Stanley Henwood, and our publications of the proceedings of the international meetings progress. In the afternoon to see the newsreels, and then to dine with Dr. and Mrs. Bela Schick at their home, where came also Drs. Karelitz, Bass, Sanger and Peshkin and the ladies.

Jan. 12—To breakfast came Bill White and Max Geffen for conferences on *Medical World News*. At noon to sit with Bill Frohlich and Dr. Greenberg for several hours, discussing trends, foreign marketing, and indeed the whole wide field of medicine. In the afternoon at the desk working on editorials. In the evening to dine with Laura and Milton Runyon at the Drake Hotel and then to see Henry Fonda and Mildred Natwick in "Critic's Choice," which is slightly lacking in action.

Jan. 13—To the National Foundation, where Tom Rivers presided, and there came Louis Flexner, Rustin McIntosh, Ed Tatum, Virginia Apgar, Catherine Worthingham, Joe Nee, Ted Boyd and others of the staff. We developed a publication project on the field of congenital malformations. Thereafter to the RCA Club, where Howard Rusk, Harold Diehl, Theodore Van Dellen, Max Geffen, Bill White and others of our staff conferred on the promotion of *Medical World News*. Then by jet from Idlewild to O'Hare in one hour and 40 minutes.

Jan. 14—In the afternoon driving to the suburbs for visits to the family, and then to dine with Ed and Bess Rosenberg. Here came many of the staff of the Weiss Memorial Hospital, including Herman Straus, Tannenbaum, Schiller and others; the

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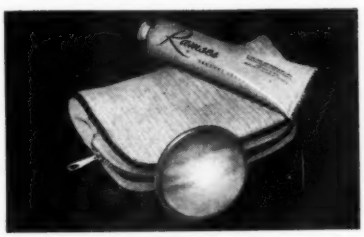

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sculptor Abbott; two architects. Cable and Pereira; the economist Nerlove, and musicians Hoffman and Kaplan, the great authority on old violins.

Jan. 15—At the desk and viewing the pro football bowl game, admiring the generalship of Unitas and Van Brocklin. Later came the Kirsners to dine.

Jan. 16—To the Tavern Club at noon to meet Drs. H. B. Parmele and Ballenger, and we discussed the physiology of rhinology. Thereafter to the desk and all the afternoon at my editorial composing. In the evening, read a new work by Irving Shulman and Peggy Bristol entitled "The Roots of Fury."

Jan. 17—At noon to Fritzel's to meet all the representatives of radio and television in Chicago who will devote much time to promoting the campaign for funds for the Chicago Heart Association. Willis Potts, Erickson and old Pepys did the speaking. Next to Roosevelt University to speak to the women's auxiliary in behalf of scholarships for medical education. In the evening to the Lake Shore Club to speak to the managers of resident hotels on medical progress.

Jan. 18—In the afternoon to autograph copies of "Heart Care" at the bookstores, and found much interest in the book. Then to the Chicago Heart Association to prepare copy for radio and television. In the evening observed on television a special play which supported the magnificent campaign of the Arthritis and Rheumatism Foundation against the development and sale of fraudulent devices. The realism made a message never to be forgotten, and the final speech by Dr. Russell L. Cecil gave it full authenticity.

Jan. 19—To the Museum of Science and Industry for a meeting of the Medical Advisory Board, and planned new exhibits on the brain, eye and other areas. The progress of science is so great that revisions of exhibits are required every five years. In the evening to hear our orchestra directed by Cluytens perform Haydn and Shostakovich.

Jan. 20—At noon to luncheon at the Tavern Club with Dr. Jordan Scher and we discussed existential psychiatry, which is one of the many movements now springing up throughout the world. In the evening observing the inaugural celebrations.

Jan. 21—At the desk until noon, when came Dr. Cogan to describe brief psychotherapy and to reminisce of the evolution of the schools of Jung, Adler. Stekel and many others. In the evening to the Phil Winstons.

Jan. 22—In the morning came Barbara to tell of current activities, and then in the afternoon to hear the Warsaw Philharmonic Orchestra in a program largely of Polish music. Thereafter to visit Grandmother Mantel, who carries her age well. Reading now "The Mozart Leaves at Nine," by Harris Greene, a realistic, exciting and convincing tale of Salzburg in the postwar period.

Jan. 23—At noon to the South Shore Country Club to speak, along with Daniel MacMaster of the Museum of Science and Industry and Robert Cromie of the *Chicago Tribune*, to the Club Managers' Association, most of them being en route to the annual session at Denver. Thereafter to my toil and read "The Health of the Presidents," by Rudolph Marx, who has some interesting facts on the lives and deaths of the presidents from Washington through Eisenhower.

Jan. 24—Early came Mr. Soldon, the new representative of the Friends of the Hebrew University. Then came Wally Ranson to lunch and to discuss the progress of books for Doubleday. In the evening to the annual meeting of the Michael Reese Hospital. Fred Mandel became president, Irving Harris was made chairman of the board, and citations were given to Grant Pick, Fred Kramer and Rachmiel Levine. Old Pepys sat with Drs. Philip Rosenblum, Leo Zimmerman and John Sheinin and the Levine family.

Jan. 25—At noon to the meeting of the Board of Governors of the Chicago Heart Association, where Vincent Cullin of the Chicago Title and Trust Company presided, and Clarence Randall of Inland Steel was elected vice-chairman. In the evening took Justin and Ann to dine and we played at bridge.

Jan. 26—At noon to the great kick-off luncheon of the Chicago Heart Association in its annual drive, with Don Erickson presiding. A program of "At Random" was staged with Irv Kupcinet as moderator and Louis Katz, Virginia Marmaduke, President Bjork of the Peoples Gas Light & Coke Company and old Pepys. In the evening to hear the Chicago Symphony Orchestra with Cluytens directing.

Jan. 27—Early to be with Don McNeill on his program. and there were some 600 young-

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sters from Grand Rapids, who added to the excitement of the occasion. At noon with Chaplain Wennerstrom and Ramsey at the University Club discussing new methods for procuring material for dissection and postmortem examination. In the evening to Art Strauss' to play at bridge with Lowell and Shapin.

Jan. 28—This day at the desk. In the evening to dine with Charles Lawrence and Epstein, the architect, and the conversation concerned philanthropy, medical practice, the history of architecture, and the European troubles.

Jan. 29—A day of rest devoted principally to more writing and to reading the report of the Ford Foundation, in which the opening statement by Dr. Henry T. Heald is a profound philosophical concept of relations of philanthropy, foundations and government. Read also "Growing Up Absurd," which is to some extent an explanation of juvenile delinquency.

A NOTE FROM HUBERT A. ROYSTER

Of all sad words of tongue or pen
The saddest are these: It might have been,
But still more sad we daily see:
It is, but hadn't ought to be.

* * *

Jan. 30—In the afternoon to meet with Ilza Veith and the committee for the program of the American Society of Medical History, which will meet in Chicago in May. Among others, Walter Alvarez will speak on medicine in Hawaii and Mexico, old Pepys will talk on great medical editors, and George Rosen will give the Garrison lecture on the dance frenzy during various epochs in history.

Jan. 31—In the morning came several podiatrists led by Dr. M. R. Lewis to discuss the building of a center for this science in the medical center of Chicago. In the afternoon at Northwestern University to give a lecture at Thorne Hall honoring the great Robert Zeit under the auspices of the Alpha Kappa Kappa fraternity. Old Pepys spoke on 50 years of medicine and a forecast; then Sutton of the Illinois State Department of Health lectured on its organization. Thereafter, to dine with the young men of the chapter, and then to attend a meeting of the Chicago Heart Association, where Robert P. Grant of the National Heart Institute spoke to the young men who are working on grants on the future of medical research.

The Medical Muse

RICHARD ARMOUR

TEMPER, TEMPER

A London psychologist, writing in *Family Doctor*, the British Medical Association magazine, says that chronic ill temper is usually deep-rooted in feelings of inferiority. —*News item.*

I never thought—I'm none too quick—
Ill temper means the temper's sick,
And though it's almost unendurable,
An ailing temper may be curable.

Since what makes people rant and rave
And gnash their teeth and misbehave
Is thinking, down deep, they're inferior,
The cure's to make them feel superior.

By drugs, hypnosis, or both mixed,
Such people's temper can be fixed.
No longer huffy, dour, and bilious,
They'll just be sweetly supercilious.

GOOD COMPANION

Finding that babies are lulled to sleep when riding in the family car, a St. Paul obstetrician has invented a gadget, a pocket-sized crib companion, that gives off the vibrations and sounds of an automobile, and he says it will keep fussy infants quiet.—*News item.*

Cuddled by his crib companion,
The blissful infant sleeps.
The gadget gives off whirs and rattles,
And screams of brakes, and beeps.

And in his dream the baby dreams
Of scenes like these, seraphic:
Chased by a speed cop, running lights.
Clamped tight amidst the traffic . . .

Now maybe nervous grownups, too,
Would find their fears subsiding,
If thus they got the sound and feel,
But never went out riding.